Does Labor Affect the Variability of Maternal Heart Rate during Induction of Epidural Anesthesia?

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The potential for unintentional intravenous or subarachnoid injection of local anesthetic during induction of epidural anesthesia mandates the administration of a test dose before injection of a therapeutic dose of local anesthetic. Moore and Batra administered 0.015 mg of epinephrine iv to volunteers and sedated surgical patients. They concluded that an increase in heart rate after the injection of an epinephrine-containing test dose is both sensitive and specific for the identification of intravascular injection. Subsequently, Abraham et al. suggested 2 ml of 1.5% lidocaine in 7.5% dextrose, with 0.015 mg of epinephrine, as an ideal obstetric test dose. In contrast, we and others have noted fluctuations in the heart rates of unanesthetized laboring women, and have questioned the specificity of an increase in heart rate as an indicator of intravascular injection. We have speculated that the cyclic pain of labor is responsible for these fluctuations in maternal heart rate (MHR). However, other factors (e.g., lack of preanesthetic medication, anxiety regarding epidural catheter placement, and/or pregnancy itself) could be responsible. The purpose of this study was to compare MHR variability during induction of epidural anesthesia in women in active labor versus women undergoing elective cesarean section.

Materials and Methods

The protocol was approved by our Review Board for research involving human subjects. Each patient gave informed consent. We evaluated the heart rate patterns of two groups of parturients. The labor group included ten consecutive, healthy women who requested epidural anesthesia during active labor (≥4 cm cervical dilation). The elective cesarean group included ten consecutive, healthy women who requested epidural anesthesia for elective cesarean section. Exclusion criteria included: 1) administration of other analgesic drugs before induction of epidural anesthesia; 2) chorioamnionitis; 3) oral temperature ≥ 37.5 °C; 4) hemoglobin concentration < 10.0 gm/dl; or 5) fetal distress.

Each patient's heart rate was recorded continuously using a method previously described by us. Briefly, we used the direct ECG mode of a separate fetal monitor (Model 80-40A, Hewlett-Packard, Palo Alto, CA). One standard ECG lead was placed at the upper left sternal border, and a second lead was placed just beneath the left breast in the anterior axillary line. The lead wires were inserted into the cable block, which was strapped to the patient's arm. The monitor electronically calculated each R-R interval and provided a continuous, graphic recording of MHR.

Each patient received an intravenous bolus of ≥750 ml of lactated Ringer's solution, and was then placed in the right lateral decubitus position for insertion of a lumbar epidural catheter. Intradermal and subcutaneous infiltration was performed with a 25-gauge needle and 1.0% lidocaine. The epidural space was entered with an 18-gauge Hustead needle using a loss-of-resistance-to-air technique. A 20-gauge polyamide catheter was threaded approximately 3 cm into the epidural space, and the needle was removed. After negative aspiration, a test dose (3 ml of 0.5% bupivacaine with 1:200,000 epinephrine) was injected over 15 s. If the patient was in labor (labor group), the test dose was given immediately after a uterine contraction. Each patient remained in the right lateral decubitus position until ≥5 min after injection of the test dose. A therapeutic dose of local anesthetic (0.25% bupivacaine for the labor group and 0.5% lidocaine with 1:200,000 epinephrine for the elective cesarean group) was not injected until ≥5 min after injection of the test dose.

The time of test dose injection was noted on the MHR tracing so that we could evaluate the MHR during the 10 min before, and 5 min after, injection of the
test dose. Uterine contractions were not recorded on the MHR tracings. Subsequently, the coded MHR tracings were shuffled in random order. One of us evaluated the tracings for MHR accelerations during the 15-min study period. A MHR acceleration was defined as an increase in MHR of ≥25 beats per minute (BPM), or ≥15 s duration. One of us then estimated the MHR (to the nearest even-numbered integer) every 5 s for the 15-min study period, and recorded this information on a data sheet.

Statistical analysis included Student’s t test and Fisher exact test to compare the two groups for maternal characteristics and the number of MHR accelerations during the 15-min study period. We estimated the total variance after correcting for the mean MHR, and also after correcting for the linear relationship between MHR and cumulative time (the latter was performed to exclude a trend effect over the 15-min study period). With both estimations, we used the least-squares method, and we compared the two groups of women using the Wilcoxon two-sample test. We then attempted to separate random MHR variance ("pure noise") from systematic variance. First, we estimated the random variance using Yule-Walker equations, and again compared the two groups using the Wilcoxon test. Second, we obtained periodograms for each patient. Three periodogram cycles had lengths (3.0, 3.75, and 5.0 min) within the 3–5-min interval typically associated with cycling of uterine contractions. An F-ratio was constructed to test whether the pooled variance for those three periodogram cycles was greater for the labor group than for the elective cesarean group. P < .05 was considered significant.

RESULTS

Women in the labor group were more likely to be nulliparous (P < .05). (In our hospital, parous women uncommonly receive epidural anesthesia during labor, whereas nulliparous women rarely undergo elective cesarean section.) There was no significant difference between the two groups with regard to maternal age, gestational age, maternal weight, oral temperature, or hemoglobin concentration (table 1).

Injection of a therapeutic dose of local anesthetic resulted in a successful epidural block in each patient. Thus each catheter was presumed to have been placed extravascularly within the epidural space.

Five (50%) of the women in the labor group, versus no woman in the elective cesarean group, had at least one MHR acceleration of ≥25 BPM of ≥15 s duration during the 15-min study period (P < .05). Of those five women, two had six accelerations, one had five, one had three, and one had one acceleration. Further, four of those women had an acceleration during the 2-min interval after injection of the test dose, and two women had an acceleration during the first minute after injection.

The total variance (after correcting for the mean MHR, and also after performing linear regression) was greater in the labor group than in the elective cesarean group (P < .05). The random variance did not significantly differ between the two groups. However, the variance associated with the 3–5-min cycles of MHR was significantly greater for the labor group than for the elective cesarean group (P < .0001).

DISCUSSION

We may be criticized for giving 3 ml of 0.5% bupivacaine as a test dose. Indeed, 15 mg of bupivacaine exceeds the recommended intrathecal dosage of bupivacaine for cesarean section. Subsequent to this study, we have replaced the bupivacaine test dose with a test dose which includes 45 mg of lidocaine.

We and others have criticized the epinephrine-containing test dose for its potential to decrease uterine blood flow and precipitate fetal distress. Further, there is concern regarding the hemodynamic response to intravascular injection of epinephrine in hypertensive parturients. Rebuttal of these criticisms includes the following arguments. First, decreases in uterine blood flow noted in pregnant sheep and guinea pigs were transient. Similar transient declines in perfusion undoubtedly occur during normal uterine contractions. Second, the adverse consequences to mother and fetus of unrecognized intravenous injection of a therapeutic dose of local anesthetic would likely be more severe. And, third, there has been no published report of adverse neonatal outcome after intravenous injection of an epinephrine-containing test dose.

In our judgement, a greater limitation of the epinephrine-containing test dose is the difficulty in inter-
preting changes in MHR during active labor. Moore and Batra\textsuperscript{a} administered 0.015 mg of epinephrine intravenously to volunteers and sedated, nonpregnant surgical patients. Abraham et al.\textsuperscript{a} administered an epinephrine-containing test dose to 250 obstetric patients. They monitored MHR "by palpation of the radial pulse or by ECG monitoring," and they observed no increases in MHR of >17 BPM in the first minute after injection in the 232 parturients who developed an objective sensory block. Their lack of false-positives may be attributed to one or both of two factors. First, if a patient was in labor, they "waited until just after a contraction to inject the test dose." Although they monitored MHR for 2 min after injection, they reported MHR changes during the first minute only, and probably missed MHR changes with subsequent contractions. Second, their patients may not have been in active labor. Although they included an unspecified number of laboring women in their study population, they waited at least 20 min after injecting the test dose before injecting a therapeutic dose of local anesthetic. Their ability to wait ≥20 min before injecting a therapeutic dose suggests that some of their patients may have been in early, latent phase labor rather than active phase labor.

In contrast, Cartwright et al.\textsuperscript{b} observed an increase in MHR of 20 BPM in 24 of 100 laboring women, and an increase of 30 BPM in 12 laboring women, during the 1-min after injection of a test dose without epinephrine. They calculated that a rise in MHR during labor of 30 BPM "is likely to be associated with intravascular placement of the catheter only once in 120 cases... and still miss 50% of intravascular injections."\textsuperscript{a} Subsequently, Leighton et al.\textsuperscript{c} reported the only published study of deliberate intravenous injection of 0.015 mg of epinephrine (or placebo) to women in active labor. The fetuses of two of the ten patients who received epinephrine developed distress lasting 10–12 min. Using a baseline-to-peak MHR criterion (a ≥25 BPM increase in MHR occurring within 120 s of drug injection and lasting ≥15 s), they identified 50% of the epinephrine-group and 20% of the placebo-group patients as having received epinephrine. They retrospectively noted improved specificity and sensitivity when they used a "peak-to-peak" criterion for intravenous epinephrine injection (a ≥10 BPM increase in the maximum MHR during the 2 min after the injection over the maximum MHR during the 2 min before the injection). However, they "question[ed] the clinical usefulness of relying on such a subjective and possibly unsafe test dose to detect intravascular catheters and suggest[ed] that another marker of intravascular injection should be developed."\textsuperscript{c}

In the present study, laboring women had greater MHR variability during induction of epidural anesthes-
sia than women undergoing elective cesarean section. Further, five of the ten laboring women had one or more MHR accelerations of ≥25 BPM of ≥15 s duration. We did not observe such accelerations in women undergoing elective cesarean section, despite use of the same anesthetic technique. The present study suggests that the increased MHR variability often seen during labor is associated with cyclic uterine contractions, rather than the lack of preanesthetic medication or pregnancy itself. The present study did not address the mechanism for that increased variability (e.g., elevated catecholamines,\textsuperscript{15,16} increased metabolic demand during uterine contractions,\textsuperscript{17} and/or other factors). Use of an epinephrine-containing test dose seems appropriate before elective cesarean section. However, anesthesiologists typically give small volumes of dilute solutions of local anesthetic to laboring women, and it may be neither realistic nor necessary to exclude intravascular cannulation with a single test dose in such cases. We believe that every dose should be a "test dose" in laboring women. Meanwhile, another indicator of intravascular injection should be developed for use during labor.

\section*{References}

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Effect of Epinephrine Concentration on Lidocaine Disposition during Epidural Anesthesia

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The advantages of adding epinephrine to local anesthetics are a more intense block, a greater duration of anesthesia, and a reduction of systemic toxic reactions.1-5 However, the cardiovascular responses caused by epinephrine absorbed from the injection site into the systemic circulation may be not always desirable.6,7 In general, the concentration of additional epinephrine should be kept at the minimal effective level.2 With respect to epidural anesthesia, the recommended concentration of epinephrine that should be added is 1:200,000.5,6 However, this preparation may be accompanied by some clinically unwanted effects of epinephrine.

The blood concentration-versus-time profile of local anesthetic serves as an index of systemic toxicity, and reflects the amount of drug remaining at the site of injection.7-9 Therefore, measurement of the blood concentration of a local anesthetic is of potential value in defining both the safety and the efficacy of a regional anesthetic procedure.7-8

In this study, we measured arterial serum concentrations of lidocaine and observed clinical responses when different concentrations of epinephrine were added to lidocaine HCl during epidural anesthesia. The results suggest that the appropriate concentration of epinephrine in epidural lidocaine is 1:600,000 or less.

MATERIALS AND METHODS

Forty female patients, classified ASA physical status 1, scheduled for either abdominal hysterectomy or abdominal hysterectomy were studied. The research protocol was approved by our Institutional Review Board, and informed consent was obtained from each patient. The patients were randomly divided into four groups of ten each, and the anesthesiologists were unaware of which concentration of epinephrine was being used in a given patient.

All patients were premedicated with atropine sulfate 0.5 mg im, hydroxyzine hydrochloride 50 mg im, and pentazocine 30 mg im 30 min before arrival in the operating room. A catheter was introduced into the radial artery for blood sampling, and the cephalic vein on the opposite arm was catheterized for intravenous infusion of Ringer's lactate solution. With the patient in a lateral decubitus position, a Tuohy needle was introduced after 0.5% procaine HCl anesthesia via the median approach at L2-3 into the epidural space, and an epidural catheter was introduced approximately 5 cm cephalad. Following 15 min, control measurements were made. Group 1, 2, 3, and 4 received 15 ml of 2%