Pregnancy Increases Median Nerve Susceptibility to Lidocaine

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To determine whether pregnancy renders women more sensitive to local anesthetics, nine nonpregnant and nine pregnant (third trimester) women underwent median nerve block at the wrist using 1% lidocaine HCl. Inhibition of median nerve Aα sensory and motor fibers was assessed using measurements of sensory nerve action potential (SNAP) amplitude and compound motor action potential (CMAP) amplitude, respectively. Inhibition of median nerve C fibers was assessed by the increase in skin temperature and by the decrease in median (relative to ulnar) galvanic skin potential (GSP) amplitude. Lidocaine inhibited SNAP to a greater extent in pregnant than nonpregnant women at all time points (P = 0.019). CMAP declined differently in the pregnant and nonpregnant groups (P = 0.01); the pregnant subjects achieved steady state inhibition before the nonpregnant subjects. The two groups developed comparable steady state inhibition. Skin temperature was higher in pregnant women at all time points (P < 0.001); moreover, the increased skin temperature of pregnant women differed from that of the nonpregnant women (P = 0.037), reflecting a more rapid temperature increase in the pregnant women. GSP amplitude declined to 50% of control more rapidly in pregnant (mean = 4 min) than nonpregnant women (mean = 11.5 min), but these differences did not achieve statistical significance. It is concluded that pregnancy increases median nerve susceptibility to lidocaine. (Key words: Anesthetics, local; lidocaine. Nerve: axon; impulse conduction. Pregnancy.)

Based on studies demonstrating higher dermatomal levels of block during pregnancy,¹ ² clinicians often administer a reduced volume of local anesthetic to pregnant patients for epidural or spinal anesthesia.³ Whether pregnant women are truly more susceptible to conduction anesthesia,⁴ and if they are, whether this alteration results from pregnancy-induced reductions in the concentration of local anesthetic required to inhibit individual spinal nerves, or from pregnancy-induced changes in the distribution of anesthetic within the spinal canal (e.g., as a consequence of epidural vein distention) remains unclear. Although Datta et al.⁵ ⁶ have shown augmented local anesthetic inhibition of rabbit nerves during pregnancy, no studies have demonstrated increased sensitivity of human nerve fibers per se to local anesthetic during pregnancy.

The present study compares median nerve block at the wrist in pregnant and nonpregnant volunteers. Our data suggest that pregnancy renders median nerve sensory fibers more susceptible to the effects of 1% lidocaine HCl.

Materials and Methods

After review and approval of our protocol by our Clinical Research Practices Committee, nine nonpregnant and nine pregnant (third trimester) volunteers gave informed consent to a study of median nerve block. Pregnant and nonpregnant subjects were studied concurrently. No subject had clinical or electrodiagnostic findings suggestive of median nerve dysfunction. Function of median Aα sensory and motor nerve fibers was assessed using antidromic sensory nerve action potentials (SNAP) and orthodromic compound motor action potentials (CMAP), respectively.⁷ Supramaximal electrical stimulation of the median nerve 2 cm proximal to the site of anesthetic injection simultaneously elicited CMAP and SNAP. Ring electrodes at the base and distal end of the middle finger recorded SNAP while abductor pollicis brevis belly tendon surface electrodes recorded CMAP. In a few subjects light touch sensibility was assessed with von Frey hairs.⁸ These plastic monofilaments consistently deliver no more than a given force before bending and have been used for nearly a century to carefully define light touch sensibility in humans.

Measurements of skin temperature (ST) and of galvanic skin potentials (GSP) elicited by a deep breath or by electrical nerve stimulation served to assess unmyelinated (C) fiber function.⁹ The GSP was recorded in a median distribution with the active electrode over the distal finger-pad of the middle finger, the reference electrode over the volar aspect of the distal interphalangeal joint, and simultaneously in an ulnar distribution with electrodes affixed to homologous sites on the fifth finger. Because the GSP response habituates with time (i.e., decreases in amplitude), we used a comparison technique (see Butterworth et al.¹⁰ for a discussion of GSP habituation). Inhibition of the median distribution GSP by local anesthetics was measured as a decline in the ratio of median/ulnar or to ulnar GSP amplitude rather than as an absolute decline in the amplitude of the median distribution GSP. A Nicolet (Madison, Wisconsin) Viking® electrodiagnostic instrument recorded SNAP, CMAP, and ST. GSP were recorded on a Grass (Quincy, Massachusetts) polygraph.
with the low frequency filter cutoff set for 1.6 Hz, following the techniques described by Low. A thermistor accurate to 0.1° C measured ST at baseline and at frequent intervals during the study over the fingertips of the third (middle) finger.

After recording baseline data and after washing the skin with isopropanol, the block was performed without seeking paresthesias by inserting a 22-G needle just lateral to the palmaris longus tendon and subjacent to the flexor retinaculum. When paresthesias occurred, the needle was repositioned. Five milliliters of 1% lidocaine HCl solution was injected over no less than 45 s. Both dominant and nondominant hands were studied. Data are presented as mean ± SEM of the pooled data. Analysis of variance for repeated measures was used to assess the effects of time (from injection of the anesthetic), pregnant status, and any possible interaction between the two factors. Comparison of GSP response of pregnant and nonpregnant subjects was accomplished using the log-rank test. Control data from some of the nonpregnant subjects were included in a previous study.

Results

One nonpregnant subject chose not to complete the experiment; therefore, the statistical analysis includes data from only 17 subjects. The SNAP amplitude declined significantly with time (P < 0.001) (fig. 1) in both groups, and the pregnant women demonstrated consistently greater inhibition at all time points (P = 0.019). The SNAP amplitude correlated inversely with light touch sensitivity as assessed with von Frey hairs (fig. 2) in both pregnant and nonpregnant subjects.

The CMAP amplitude declined significantly after lidocaine injection in a time-related fashion in both pregnant (P = 0.005) and nonpregnant women (P < 0.0001) (fig. 3). Although pregnant women achieved steady state levels of block faster overall (P = 0.012), between-group differences did not achieve statistical significance at any individual time point.

ST increased significantly in both pregnant (P < 0.0001) and nonpregnant women (P = 0.028) (fig. 4). As expected from prior studies, the pregnant women had higher ST at baseline and higher overall ST (P < 0.0001). Although small in amplitude, the increase in ST was highly consistent (ST increased in every pregnant...
woman) and more rapid \((P = 0.037)\) in pregnant women. The nonpregnant subjects demonstrated a consistent decrease in ST shortly after injection of the local anesthetic, which we attribute to relative hypoperfusion of the hand from pain associated with the injection.\(^{12}\) Pregnant women did not demonstrate this response.

GSP amplitude declined by 50% in a mean time of 4 min in the pregnant group compared with 11.5 min in the nonpregnant group (fig. 5), but these differences did not achieve statistical significance (using the log-rank test).

**Discussion**

Our data suggest that the median nerve of women during the third trimester of pregnancy is more susceptible to block by lidocaine than is the median nerve of nonpregnant women. This confirms the *in vitro* findings of Datta *et al.*\(^5\) and Flanagan *et al.*\(^6\) showing that vagus nerves removed from pregnant rabbits are more susceptible to local anesthetic-induced conduction block and represents the first evidence that pregnancy renders mammalian peripheral nerves more susceptible to local anesthetics.

We used objective measures of nerve fiber function to precisely quantitate the extent of failure of impulse conduction. The techniques we employed represent standard electrodiagnostic tests of peripheral nerve function\(^7\) that are used to evaluate peripheral nerve lesions. In marked contrast to these objective methods, clinical evaluation of sensory function does not readily lend itself to quantitative analysis. Although the degree of depression of SNAP correlated with inhibition of somesthetic perception (fig. 1), our experimental subjects had difficulty defining the degree of their sensory impairment after injection of lidocaine. Furthermore, clinical testing of motor and autonomic function is particularly problematic. Thus, we considered that the objective, electrodiagnostic methods we used more effectively and accurately detected pregnancy-related changes in the rate and extent of impulse blockade due to lidocaine.

Our study was not designed to determine the cellular mechanism of increased local anesthetic susceptibility due to pregnancy; however, we speculate that an alteration in the local anesthetic binding site on the Na\(^+\) channel could produce an increased affinity for local anesthetic molecules. (Most agents that alter local anesthetic binding to Na\(^+\) channels decrease local anesthetic affinity for the channel.\(^{13}\) Alternatively, minor changes in the myelination of peripheral nerve might decrease the critical length of anesthetic exposure,\(^{14}\) and ultimately, decrease the minimal anesthetic concentration for inhibition of impulse conduction *via* myelinated fibers. In either case, we speculate that increased concentrations of progesterone (or some other pregnancy-related hormone) underlie pregnancy-induced increased local anesthetic susceptibility. Supporting our hypothesis, Flanagan *et al.* have replicated the increased local anesthetic susceptibility of pregnancy by administering progesterone to nonpregnant rabbits.\(^{15}\)

Our data suggest a neural cause for the increased spread of epidural anesthesia in pregnant women detected by Bromage\(^1\) and Fagreus *et al.*\(^2\) Although distention of the lumbar epidural venous plexus and displacement of
the local anesthetic solution to more cranial regions of the spinal canal may occur, our data argue that individual spinal nerves are inhibited by lower concentrations of local anesthetics during pregnancy.

Pregnancy, in addition to altering local anesthetic susceptibility, may decrease the MAC for volatile anesthetics. If our axon-based theory for general anesthesia is correct, the increased susceptibility to local anesthetic inhibition we observed may also underlie pregnancy-induced decreases in MAC. Indeed, Datta et al. have replicated the decreased MAC of pregnancy by administering progesterone.

We conclude that pregnancy potentiates lidocaine inhibition of impulse conduction in median nerve fibers. Whether this increased susceptibility results from alterations in impulse conduction and conduction safety or from increased local anesthetic affinity for the Na⁺ channel remains to be determined.

The authors wish to thank Faith McLellan for editorial advice, Debbie Wood for assistance with electrodiagnostic studies, and Joni Brockschmidt, Department of Public Health Sciences, for her assistance with the statistical analysis.

References