

Title: EFFECT OF EXOGENOUSLY ADMINISTERED PROGESTERONE ON SUSCEPTIBILITY OF RABBIT VAGUS NERVES TO BUPIVACAINE.

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Introduction: A faster onset and a higher spread of epidural anesthesia have been observed in pregnant patients (8-12 weeks) compared to non-pregnant individuals of same age¹. Hormonal changes during pregnancy may alter the susceptibility of neural tissue to local anesthetics and thus explain the differences observed. Previous studies have shown that bupivacaine caused a more rapid onset and a more profound degree of conduction block in isolated nerves from pregnant animals as compared to nerves from non-pregnant animals^{2,3}. Higher progesterone concentrations may be responsible for the enhanced conduction block observed in nerves from pregnant animals. This study was undertaken to assess the effect of exogenous progesterone in combination with bupivacaine on the compound action potential (CAP) of vagus nerves from ovariectomized rabbits.

Materials and Methods: 51 vagus nerves obtained from New Zealand female white rabbits (4-5 kg) were used for this study. Animals were housed in an NIH approved Animal Care Facility and were sacrificed in accordance with the guidelines for the care and use of laboratory animals. Group A consists of 17 nerves from intact animals. Group B contained 17 nerves obtained from ovariectomized rabbits injected with peanut oil. Group C consisted of 17 nerves from ovariectomized rabbits treated with progesterone (30 mg/kg) in peanut oil. The latter two groups were injected intramuscularly for a period of 4 days. Intact sheath nerves were removed, transferred to the electrode chamber and baseline CAP were recorded at a stimulus rate of .017 Hz. The nerves were then bathed with bupivacaine concentrations of 0.1 mM, 0.15 mM, or 0.2 mM until a steady-state CAP level was attained (not more than 10% difference in the amplitude within 5 minutes). The nerves were then washed with HEPES Liley solution and the minimum time for 85% recovery of control CAP in all fibers was recorded. Plasma progesterone levels were measured in 21 animals prior to sacrifice. Linear regressions were determined via least squares analysis. Analysis of covariance was employed to assess differences between the groups. Statistical significance was assumed with P values less than 0.05.

Results: The reduction in CAP amplitude in A-, B- and C-fibers was not

different between intact animals and animals treated with peanut oil. However, the percentage depression of CAP was significantly higher in all the fiber groups in animals treated with progesterone (Table I). The time for the recovery of CAP amplitudes was also significantly longer in animals who received progesterone. As expected the progesterone concentrations were higher in this group (Table 2).

Discussion: The results show that exogenous progesterone increases the susceptibility of the vagus nerve to different concentrations of bupivacaine. This increase susceptibility may be related to: a) alterations in local anesthetic diffusion through the nerve sheath and/or b) actual change in membrane sensitivity to local anesthetics.

References:

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(Experimental (C_M for Nerve Fibers)
Group)

	A	B	C
intact	.173	.184	.190
oil	.195	.177	.211
progesterone in oil	.138	.139	.142

TABLE 1: The relationship between C_m and experimental group. C_m is calculated from the respective linear regressions as the concentration (mM) of bupivacaine required for 50% conduction blockade.

	mean plasma progesterone concentration	recovery time
intact	2.7 ± 0.5	36.3 ± 2.5
oil	4.3 ± 1.2	33.3 ± 1.4
progesterone in oil	82.3 ± 14.8	81.4 ± 5.1

TABLE 2: Data for plasma progesterone (ng/ml ± S.E.) and recovery time (minutes ± S.E.).