

Title: DIFFERENTIAL SENSITIVITY OF FIBERS IN MAMMALIAN NERVE
ONSET AND OFFSET OF LOCAL ANESTHETIC BLOCK

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INTRODUCTION

Greater clinical use of local anesthetic (LA) agents has been limited by the unpredictability of the duration of any specific surgical procedure, by the question of the adequacy of a single dose of LA to provide sufficient surgical anesthesia time, by the slow recovery of nerve function and the constant concern of general LA toxicity.

With these goals in mind we examined the differential behavior of fast and slow fibers in the isolated nerve with the pre-conditions that (1) all nerve fiber groups (A, B, and C) be 100% blocked in less than 10 minutes, (2) recovery to 50% of function in all nerve fibers should occur in less than 30 minutes and, (3) the above to be done with minimum drug concentration.

METHODS

The methods used have been presented in detail in a previous publication on the differential sensitivity of fast and slow fibers in peripheral nerve¹. We used intact isolated rabbit vagus nerve at room temperature perfused by HEPES-Liley (HEPES-L) solution at the indicated pH at a rate of 0.1 ml/minute. Bupivacaine HCl and lidocaine HCl were dissolved in HEPES-L solution for each days experiment. A single nerve was used for each drug concentration, each nerve was used on the day of dissection and stored in HEPES-L solution continuously aerated by 100% O₂.

RESULTS

Since we desired rapid block at minimal drug concentration we used alkaline HEPES-L (pH 7.8). Equivalent block in acid media (pH 6.9) required a five fold increase in drug concentration. Continuous application of bupivacaine at 2.5 mM (pH 7.8) showed a markedly delayed recovery during the wash period. Application of a lower drug concentration allowed rapid recovery but demonstrated prolonged onset. The combination of bupivacaine at 2.5 mM for 10 minutes followed by 0.125 mM (both at pH 7.8) for 60 minutes gave 100% block for the period of LA application and the desired rapid recovery during wash. It also seemed that decreasing the pH of the wash media (pH 7.4) facilitated recovery.

The ratio of drug concentration for induction and maintenance was 20/1 using bupivacaine. With lidocaine the ratio was 4-5/1.

DISCUSSION AND CONCLUSIONS

These experiments indicate that the best method of administering LA is by continuous or intermittent doses, rather than one single bolus. The anesthetic technique should include a catheter, placed close to the nerve supplying the surgical area (eg. by the method of P. Raj²). The induction dose of LA should be small and concentrated and in an alkaline media and block should be maintained by a lower concentration repeated for the duration of the procedure as necessary. At the completion of the surgery wash solution (free of LA drug) and of a lower pH should be introduced through the catheter to facilitate recovery. LA drugs for clinical use should be

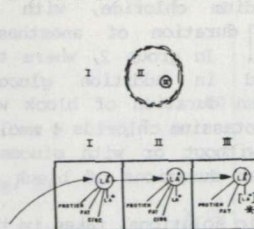
dissolved in alkaline media and should also be available at various concentrations to the anesthesiologist.

We believe the induction/maintenance ratios for bupivacaine and lidocaine represent the different lipid solubilities of the two drugs and that there are significant non-reactant fat soluble depots in the nerve trunk. Before the neutral LA molecule (the permeant form) can reach the inside of the nerve fiber it must traverse an outside tissue compartment surrounding the nerve fiber. With this kinetic model the concentration of uncharged LA determines the rapidity of onset of nerve block. The offset of block is dependent on drug lipid solubility and the saturation of non-reactive depot. A very close analogy can be made to the kinetics of uptake of gaseous anesthetics³. Lidocaine (with low lipid solubility) would be analogous to N₂O and show rapid onset. Bupivacaine would be analogous to ether and show slow onset. As with ether, onset can be accelerated with bupivacaine by the short use of a high concentration.

REFERENCES

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UPTAKE of LOCAL ANESTHETIC



UPTAKE of GAS ANESTHETIC

