Title: EFFECTS OF PH-ADJUSTED LIDOCAINE SOLUTIONS ON THE COMPOUND ACTION POTENTIAL IN INTACT RAT SCIATIC NERVES

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INTRODUCTION

Some regional anesthetic techniques have a limited role in clinical practice due in part to the length of time required to achieve a surgical level of anesthesia. Alkalinization of local anesthetic solutions has been reported to speed the onset of anesthesia (1), however other studies have produced varying results. Most local anesthetics are secondary or tertiary amines existing in equilibrium between a charged and neutral form depending on the pH of the solution and the pK_a of the specific molecule. The neutral form, being lipid soluble, should freely diffuse across tissue barriers gaining access to the axon. Thus with more alkaline solutions, the increased ratio of neutral to charged species should result in a more rapid uptake of the drug (2).

Because of the disparity found among the various clinical studies, the following study was undertaken to develop a simple paradigm to test local anesthetic solutions using the rat sciatic nerve.

METHODS

This double-blinded randomized study was carried out on twelve 180-225g female Sprague-Dawley rats. Sciatic nerves were exposed and a trough was formed, isolating a 1 cm portion of the nerve using Parafilm and petroleum jelly. Compound action potential (CAP) recordings were obtained in retrograde fashion with a stimulating electrode placed distally on the tibial nerve and a recording electrode placed proximally on the sciatic nerve. The nerve was stimulated with a 50 μsec pulse once per second to obtain a reproducible CAP tracing on the oscilloscope. Criteria for inclusion in the study were: original CAP amplitude $\geq$ 100 mV with a maximal amplitude threshold of $\leq$ 6V, a non-leaking trough, and rat body temperature $\geq$ 35 °C. Each nerve (18 total) was then randomly assigned to a group receiving 100 μl of the following solutions: A) 15 μl of normal saline per ml of 5 mM lidocaine (pH 6.00), B) 15 μl of 1.0 M $NaHCO_3$ per ml of 5 mM lidocaine (pH 7.05), C) 15 μl of 1.3 M $NaHCO_3$ per ml of 5 mM lidocaine (pH 7.55). CAP amplitudes were recorded at 10 sec intervals up to 5 min. At the completion of each experiment, a baseline was established by the addition of 2% lidocaine to achieve a complete block. Data were plotted and analyzed by linear correlation and regression to determine the time to onset of nerve block, arbitrarily defined here as the time required to obtain half the amplitude of the original CAP. These times were then compared using two-tailed t-tests corrected for multiple comparisons using the method of Bonferroni.

RESULTS

The time to onset of nerve block decreased with increasing pH of the lidocaine solutions tested (Fig. 1). In group A, the average time (± SD) required for onset of nerve block was 203.4 ± 63.8 sec, in group B the average time was 134.2 ± 36.9 sec, and in group C the average time was 103.3 ± 25.0 sec. The latency to conduction block was significantly greater in the low pH group (A) then in the high pH group (C) ($p<0.05$).

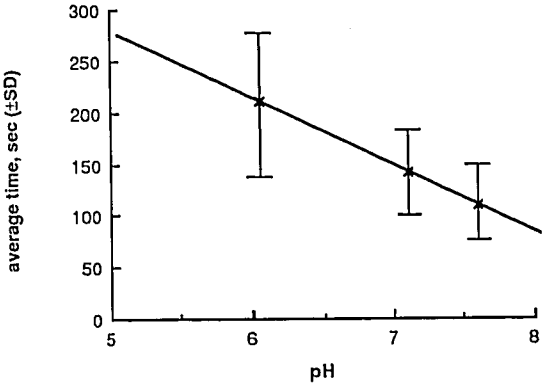

Fig 1. The average time to onset of nerve block, calculated by linear correlation and regression analysis performed on data obtained from each nerve, vs pH of lidocaine solution.

DISCUSSION

These results are consistent with the thesis that alkalinization of local anesthetic solutions decreases latency to onset of nerve block. We have shown a significant difference between unbuffered lidocaine solutions and solutions adjusted to more physiologic pH's. One would expect that commercially-prepared lidocaine solutions containing epinephrine would have an even longer latency to nerve block as these solutions are prepared at lower pH to prevent catecholamine oxidation (3). However, extrapolation of these results to clinical scenarios must be done with caution. The present methods are controlled much more easily than would be possible in the clinical environment, thus these results may not be reproducible in practice. In absolute terms, the largest differences observed in this study were on the order of a few minutes, which on average may not justify the potential risks of routinely preparing these solutions.

Previous clinical studies using local anesthetic solutions buffered by CO_2 or HCO_3^- have produced varying results at least in part due to interoperator variability, anatomic variations between subjects, and at best, indirect evidence of localization of solutions to perineuronal spaces. The methods used in this study provide a simple animal model useful for assessing the efficacy of various local anesthetic solutions with the advantage of allowing direct visualization and application of solutions to the nerve.

REFERENCES

1. DiFazio CA, Carron H, Grosslight KR, Moscicki JC, Bolding WR, John RA. Comparison of pH-adjusted lidocaine solutions for epidural anesthesia. *Anesth. Analg.* 65: 750-4, 1986.

2. Ritchie JM, Ritchie B, Greengard P. The active structure of local anesthetics. *J. Pharm. Exp. Ther.* 150: 152-9, 1965.

3. Moore DC. The pH of local anesthetic solutions. *Anesth. Analg.* 60: 933-4, 1981.