Title : MIXTURES OF LOCAL ANESTHETICS: BUPIVACAINE-CHLOROPROCAINE

Authors : A. Galindo, M.D., Ph.D., and T. Witcher, B.S.

Affiliation: Department of Anesthesia, University of Miami School of Medicine, Miami, Florida 33101

Introduction. The mixture of an anesthetic of short duration and rapid onset, such as chloroprocaine, with one of long duration, but slow onset, such as bupivacaine is said to induce a nerve block having the best characteristics of the individual agents (1), however, others have failed to confirm this observation (2). Mixing anesthetic solutions, commercially prepared to be used as individual agents, may alter the ideal pH for one or both of them (3). Anesthetics might also compete for receptor sites, with one agent dominating the ensuing block. The objective of this work was to determine, under laboratory controls, the characteristics of nerve blocks produced by chloroprocaine and bupivacaine alone and in combination.

Methods. Thirty-six experiments were performed on rat sciatic nerve preparations. Rats were anesthetized with intraperitoneal pentobarbital, paralyzed with gallamine triethiodide (Flaxedil) and ventilated with a small animal respirator (Harvard). Both sciatic nerves were dissected with special care to preserve their blood supply. Temperature of the preparation was maintained at $35^{\circ} \pm 1^{\circ}C$.

The anesthetics were applied to a 3 mm segment of the sciatic nerve for a period of 10 minutes followed by washout with warm Ringer's solution. Changes in the amplitude of the nerve action potential, in response to suprathreshold electrical stimulation, were used to determine the effects of the commercially available solutions of, chloroprocaine 1% (Nesacaine, Pennwalt), pH 3.56. Bupivacaine 0.25% (Marcaine, Winthrop) pH 5.60; a mixture of equal parts of chloroprocaine 2% and bupivacaine 0.5%, pH 3.60; sodium bicarbonate was added to this mixture as needed to obtain a pH of 5.56 in a fourth group of experiments. The results were plotted as percentage depression vs. time; separate regressions for each experiment were run over the recovery period between 5 and 30 minutes. These regressions were grouped together for all experiments within each treatment group to obtain a common slope; the groups slopes were compared by analysis of covariance (Figure).

Results. The nerve block observed under the combination of commerically available chloroprocaine-bupivacaine resembled that obtained with chloroprocaine alone, displaying a rapid onset and short duration; the long duration block characteristic of bupivacaine was not observed. Correction of the pH of the mixture from 3.6 to 5.56 changed the type of nerve block to one of faster onset and slower rate of recovery (Figure).

Discussion. Combining commerically available anesthetic solutions may not result in the theoretical advantages suggested from single drug effects. Study of a given mixture should be performed first under controlled laboratory conditions to determine the requirements needed to achieve these theoretical predictions. Other variables not readily controlled in clinical practice may affect results obtained with anesthetic mixtures in an unpredictable manner.

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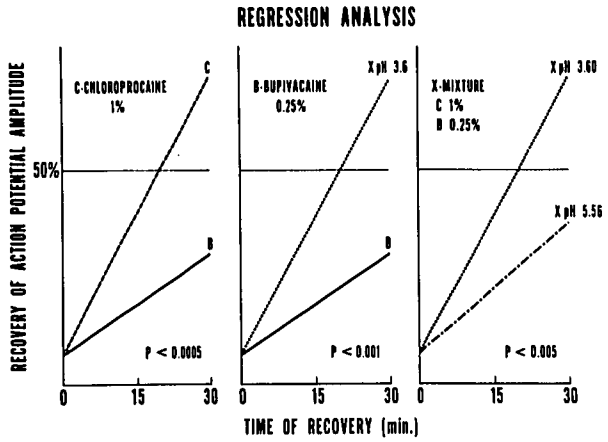

Normalized regression analysis of the rate of recovery of the sciatic nerve action potential. This rate was significantly faster following 10 minutes of application of commercially available chloroprocaine 1% (C) or the mixture of chloroprocaine 1%-bupivacaine 0.25% (X) at pH 3.60, than with bupivacaine 0.25% (B) alone or in combination with chloroprocaine 1%, but with a corrected pH of 5.56.