Title: THE EFFECT OF pH ADJUSTMENT OF BUPIVACAINE ON EPIDURAL ANESTHESIA FOR CESAREAN SECTION

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Introduction: In 1960, Loder reported that a longer duration of action of intercostal nerve block resulted from the addition of dextran to the local anesthetic.[1] Rosenblatt subsequently suggested that the factor influencing the duration of action of nerve blocks might be the pH of dextran 40.[2] The effect of raising the pH of local anesthetics, on quality and duration of block, was confirmed by Galindo.[3] A previous study, in this institution, of pH adjustment of low doses of 0.25% bupivacaine (Marcaine^R), prior to epidural injection in parturients, showed a significant increase in the speed of onset and duration of labor analgesia.[4] This double-blind study was undertaken to assess the effect of raising the pH of 0.5% bupivacaine to $\geqslant$ 7, immediately prior to epidural anesthesia for Cesarean section, after obtaining approval from the Clinical Screening Committee for Research Involving Human Subjects, of the University of British Columbia.

Methods: Informed consent was obtained from 80 A.S.A. Class 1 patients who were scheduled for elective Cesarean section under epidural anesthesia. Each patient received an intravenous infusion of 1000-1500 ml Ringer's lactate solution. An epidural catheter was inserted at L2/3 or L3/4 level and threaded 2-3 cm cephalad. The patients were randomly assigned to one of two groups, to receive either the standard commercial preparation, or pH adjusted, 0.5% bupivacaine. Both the investigator and the patient were blinded to pH of the local anesthetic used. The pH adjusted bupivacaine was freshly prepared by the addition of 0.1 ml of 8.4% (w/v) sodium bicarbonate to 20 ml of 0.5% bupivacaine. A "test dose" of 3 ml was followed by 5 ml increments, to produce anesthesia to T4 level. Because of the study protocol, epinephrine was not used in the test dose. The time of injection of the test dose was regarded as "zero" time. The time of onset was measured by loss of temperature sensation (to ice) at L1 level. Time to peak effect was recorded as the time to sensory loss (to ice) at the highest segment reached. Loss of temperature sensation was also recorded in the S_2 segment. The duration of the block was recorded as the time to regression by 2 segments, as evidenced by return of temperature sensation. The quality of the block was judged by the need for supplemental intravenous narcotic (fentanyl) during the surgery. The pH of the bupivacaine was measured, using a digital pH meter, within 30 minutes of pH adjustment.

A further 20 patients (10 in each group) were studied in the same manner, with addition of 1:400,000 epinephrine to the local anesthetic solution.

Results: The pH of the standard preparation of bupivacaine was 5.49 ± 0.86 (SEM) and that of the pH adjusted solution was 7.04 ± 1.1. Raising the pH of the local anesthetic resulted in significant shortening of the time of onset, time to block of the S_2 segment and time to peak effect. Duration of the block was lengthened from 124.8 ± 4.86 minutes, in the control group, to 147.3 ± 4.38 minutes. (Table I) The intensity of the block was not affected by pH adjustment of bupivacaine and the total bupivacaine dose was similar in both groups.

The addition of 1:400,000 epinephrine to bupivacaine did not significantly affect these results.

Discussion: Most local anesthetics are marketed as mildly acidic hydrochloride salts, to improve solubility. Raising the pH of the solution, prior to injection, will increase the amount of base available for diffusion through axonal membranes. While the long duration of action of bupivacaine is usually a desirable feature of the drug, the slow onset of action is a disadvantage. Raising the pH of the solution, immediately prior to injection, will significantly shorten the onset time and allow the surgery to proceed more rapidly. The S_2 segment is said to be the most difficult to block in epidural anesthesia and this study has shown a significant shortening of onset of anesthesia at this segment.

TABLE I

	Standard bupivacaine	pH adjusted bupivacaine
pH	5.49 ± 0.86	7.04 ± 1.1 *
Onset time (mins)	6.4 ± 0.34	3.18 ± 0.18 *
S_2 onset time (mins)	13.5 ± 0.82	8.63 ± 0.58 *
Time to peak effect (mins)	24.8 ± 1.04	18.08 ± 0.8 *
Duration (mins)	124.8 ± 4.86	147.3 ± 4.38 +
Bupivacaine dose (mg)	97.38 ± 2.3	95.88 ± 1.96

All values expressed as Mean ± S.E.M. * p = < 0.001 + p = < 0.01

References:
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