TITLE: TONIC AND PHASIC LOCAL ANESTHETIC EFFECTS IN RAT HIPPOCAMPAL PYRAMIDAL CELLS

AUTHORS: JF Butterworth IV, MD, LR Cole, BA
AFFILIATION: Dept of Anesthesia, Wake Forest University Medical Center, Winston-Salem, North Carolina 27103

Introduction: Lidocaine is thought to block impulses in peripheral nerves by tonic inhibition of neuronal Na^+ channels and to treat ventricular arrhythmias by phasic (or use-dependent) inhibition of cardiac Na^+ channels (1). How lidocaine produces its CNS effects remains unknown. We, therefore, compared the actions of lidocaine and its quarternary derivative QX-314 on the membrane properties of rat pyramidal cells during varying rates of stimulation.
Methods: Rat hippocampal slices were prepared as previously described (2,3). A single intracellular microelectrode recording technique was used to measure firing threshold and action potential (AP) spike amplitude. Tonic and phasic block of AP spikes was measured during supramaximal stimulation at 0.1, 1, 2, & 4 Hz. Lidocaine (0.05, 0.1, 1, & 3 mM) was dissolved in artificial CSF before application; QX-314 (which is nearly membrane-impermeant) was allowed to enter the cell from the intracellular electrode. Data are reported as means+SEM.
Results: At concentrations below 1 mM, lidocaine increased tonic firing threshold without altering AP amplitude (fig 1). At concentrations of 1 mM and greater (fig 1), lidocaine both increased firing threshold and decreased APs. Phasic block was not apparent at any lidocaine concentration. Cells exposed to QX-314, in contrast to those exposed to lidocaine, demonstrated marked phasic inhibition of APs with depolarization rates >1 Hz.
Discussion: Unlike QX-314 (4) and in confirmation of previous studies (5) in other preparations, lidocaine produced negligible phasic block in brain cells. Lidocaine may have less tendency to produce phasic block of pyramidal cell APs because (due to its ionizable amine moiety) it may have multiple potential routes of egress from its binding site on the Na^+ channel (through membrane or via the aqueous, ion-conducting portion of the channel). QX-314, on the other hand, would be limited by its obligatory positive charge only to the latter pathway, an "escape" route only available during when the channel is "open". Thus, our findings would suggest that phasic inhibition of pyramidal cell APAs does not underlie the CNS effects of lidocaine. Finally, our results would argue that QX-314 inadequately models phasic lidocaine effects in brain cells.

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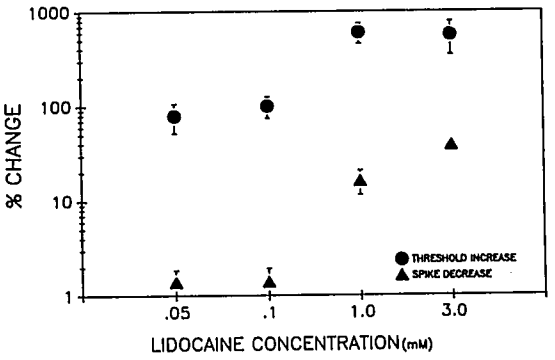


TITLE: EPIDURAL ANALGESIA PREVENTS LOSS OF LUNG VOLUME.

AUTHORS: D.N. Buckley, MD, J. MacIntosh*, MSc, W.S. Beattie, MD, J.B. Forrest, MB
AFFILIATION: Dept. Anaesthesia and Dept. Physiotherapy*, McMaster University, Hamilton, Ontario, Canada L8N 3Z5

Loss of lung volume postoperatively is well documented[1] and provision of adequate analgesia is reported to limit this phenomenon. We propose that the analgesia from epidural morphine is superior to that from parenterally administered morphine.

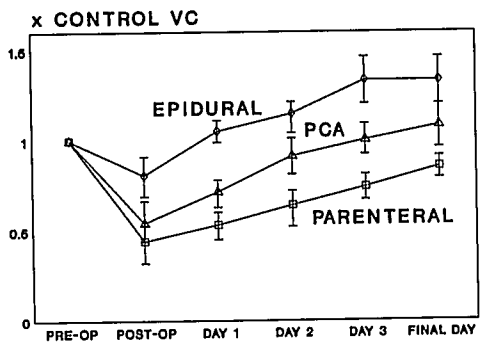
An acute pain service was instituted approximately one year prior to this data review. At the surgeon's request, postoperative analgesia was coordinated for patients undergoing major surgery. Either patient controlled analgesia (PCA) with morphine, or epidural analgesia with morphine was provided, depending on the patient, the anesthetist and the availability of equipment. Epidural analgesia involved preoperative insertion of an epidural catheter, confirmation with a test dose of local anesthetic and use of a local anesthetic for at least part of the intraoperative anesthetic. Prior to the end of surgery epidural morphine in a dose of 0.1 mg/kg was injected. A third group of patients received intermittent parenteral morphine or meperidine as required for analgesia.

The physiotherapy department measured changes in vital capacity perioperatively for patients undergoing upper abdominal surgery. This involved baseline and preoperative assessment of vital capacity, and twice daily reassessments for the first five postoperative days. For each measurement, there were two practice attempts followed by three vital capacity manoeuvres which were averaged.

Of twenty patients studied, six received epidural analgesia, seven used PCA devices and seven received intermittent IM or IV narcotics according to a prn schedule. Patients receiving prn analgesia exhibited a 53% ($p \leq 0.001$) drop in vital capacity on day 1 postop returning to 75% of baseline by the fifth day postop. Patients receiving PCA analgesia experienced a 33% ($p \leq 0.01$) drop in vital capacity on day 1 returning to baseline by the third postoperative day. There was no change in vital capacity in patients receiving epidural analgesia for up to two days postop.

These results demonstrate that analgesia improves recovery of lung function. They suggest a significant advantage for the analgesia obtained with epidural opiates because the loss of vital capacity did not occur. a prospective trial is planned to examine the differential effect of mode of analgesia of both pulmonary and cardiac complications perioperatively.

FIG. 1



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