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Title: HYPERKALEMIA AND BUPIVACAINE BLOCK OF AV CONDUCTION

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Introduction. While bupivacaine has been found to be generally safe, reports of cardiac arrest have caused concern among anesthesiologists. Of particular interest is the suspicion that these arrests may occur almost simultaneously with CNS siezures, both resulting from typical clinical doses of bupivacaine, administered inavertently intravascularly (1). These clinical observations are at variance with the results of experiments done in laboratory animals in which cardiovascular function is essentially preserved during bupivacaine-induced CNS siezures (2,3). It is possible therefore that some condition, asymptomatic in itself, has predisposed these patients to a cardiotoxic effect of relatively low plasma concentrations of bupivacaine. In view of the well known relationship between extracellular K^+ concentration and the cardiac effects of lidocaine (4) it may be that the cardiotoxicity of bupivacaine is influenced by the level of extracellular K^+. To test this possibility, we have studied the effect of bupivacaine on the function of the isolated, perfused rat heart in the presence of varying concentrations of extracellular K^+.

Methods and Materials. Isolated rat hearts were perfused in the working (left ventricular pumping) mode. The basal perfusion medium used was a modified Krebs-Henseleit bicarbonate which contained 5.9mEq/l of K^+, the normal plasma concentration of K^+ for the rat (5). Hyperkalemic media were prepared by increasing the concentration of KCl. All media were equilibrated with a gas mixture of 95% O_2, and 5% CO_2, and perfusion temperature was 37°. The ECG was measured with a pair of electrodes placed on the surface of the heart, aortic pressure was measured with a Statham pressure transducer, and all parameters were recorded on a Gilson polygraph.

Results. Bupivacaine (up to 5.0mg/l) had little effect on the aortic pressure, i.e., on the strength of individual ventricular contractions. Bupivacaine at 2.5 - 5.0mg/l slowed ventricular rate and this effect was potentiated by hyperkalemia (Fig. 1). At each concentration of bupivacaine, the potentiation by hyperkalemia was statistically significant ($p < 0.05$) as compared to the corresponding value obtained in the presence of a normal concentration (5.9mEq/l of K^+). Hyperkalemia (up to 9.0mEq/l of K^+) had no effect on the heart rate in the absence of bupivacaine. While bupivacaine slowed atrial rate, this effect was not potentiated by hyperkalemia. This indicates that hyperkalemia, in the presence of bupivacaine, acts to potentiate ventricular slowing by altering AV conduction rather than by affecting SA pacemaker activity or conduction within the atria. Bupivacaine slowed AV conduction even in the presence of a normal concentration of K^+, and hyperkalemia potentiated this effect. Hyperkalemia in the absence of bupivacaine had little effect on PR interval. The effect of K^+ on the AV conduction was found to be dependent on the concentration of bupivacaine. With 2.5mg/l of bupivacaine only 9.0mEq/l of K^+ had significant effect ($p < 0.01$ compared to bupivacaine, 2.5mg/l; K^+, 5.9mEq/l), while with bupivacaine concentration of 3.75 or 5.0mg/l the mildest hyperkalemia tested (K^+, 8.0mEq/l) had a highly significant effect ($p < 0.01$).

Discussion. The results of the present study identify mild hyperkalemia as one of the factors that potentiates the negative chronotropic effect of bupivacaine in the isolated, perfused rat heart model. Of particular interest is that the degree of hyperkalemia was such that heart function was unaffected in the absence of the local anesthetic. It should be noted that even 9.0mEq/l of K^+ is less than twice the normal K^+ concentration (5.9mEq/l) in rat plasma (5). Thus, it appears possible that inadvertent intravascular injection of clinical doses of bupivacaine in individuals with asymptomatic mild hyperkalemia could result in severe bradycardia and cardiac arrest.

References.

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Figure 1. Φ = SEM