ACCIDENTAL HYPOTHERMIA AND INTRAVENTRICULAR CONDUCTION DISORDERS INDUCED BY BUPIVACAINE

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Introduction. Bupivacaine has an inhibitory effect on ventricular conduction, which at high plasma levels (6.0 - 8.0 µg/ml) may cause life-threatening dysrhythmias. These dysrhythmias normally do not occur at the far lower bupivacaine concentrations (1.0 - 1.5 µg/ml) which usually result from the slow absorption of the drug following local or regional anesthesia (1). Thus, the occasionnal occurrence of cardiovascular accidents in association with usual doses of bupivacaine suggests the association of a factor which may enhance the conduction disorder.

Hypothermia might be this factor. Certainly, core temperature may fall in patients who are motionless, are anesthetized in operating rooms in which the temperature is less than 21° C (2), have open body cavities, and are vasodilated. If local or regional anesthesia is accompanied by general anesthesia, a fall in body temperature is inevitable. Although normal ventricular conduction usually is not seriously affected when temperature is decreased by 4° C or less (2), this may not be the case when conduction previously has been inhibited by bupivacaine. The aim of the present study was to determine if hypothermia potentiated the adverse effects of bupivacaine on ventricular conduction.

Methods. The study was carried out in 26 dogs, anesthetized with thiopental (4 mg/kg) and chloralose (80 mg/kg) and artificially ventilated to maintain normal arterial blood gases and pH. In all dogs, an extracorporeal circuit, equipped with a peristaltic pump to adjust blood flow, was interposed between the femoral artery and vein. When indicated below, this was used to reduce core temperature (measured with an electronic esophageal thermometer) from 39° to 35° C within 20 - 30 min. Three groups of dogs were studied : 1) Control-normothermia, i.e., bupivacaine alone, infused i.v. at a rate of 0.1 mg/kg/min after a loading dose of 4 mg/kg (n = 10), without cooling of the extracorporeal circuit ; 2) Hypothermia alone, 35° C (n = 6) ; and 3) Bupivacaine followed by hypothermia (n = 10), as in groups 1 and 2. Bupivacaine plasma concentrations in groups 1 and 3 were maintained between 2.0 - 3.5 µg/ml as determined by HPLC. Concentrations were sustained for 50 - 60 min in group 3 dogs before hypothermia was instituted.

Mean arterial blood pressure was continuously recorded. The duration of QRS complexes was determined by EKG. Conduction time (CT) between the base and apex of the right ventricle was measured with two endocavitary electrodes. As conduction defects are frequency-dependent, measurements of CT were made at a high pacing rate, i.e. 180/min. Effective refractory period (ERP) was measured by the extrastimulus method (3).

A paired Student's t test was used to compare, in groups 1 and 3, values under bupivacaine to control values and, in all groups, the values with extracorporeal circulation to the values immediately preceding.

Results. There were no significant changes in the duration of the QRS complexes, CT and ERP attributable to the opening of extracorporeal circuit (group 1) or hypothermia alone (group 2).

By contrast, the duration of the QRS complexes, which was lengthened from 48 ± 3 (mean ± SEM) to 63 ± 3 ms ($p < 0.01$) by bupivacaine treatment in the combined treatment group was further lengthened to 103 ± 5 ms ($p < 0.001$) by the addition of hypothermia. However, the direct effect on this parameter was counteracted by concomitant bradycardia (154 ± 7 to 112 ± 6 beats/min) ($p < 0.001$). When paced at a rate of 180 bpm, the change in CT due to hypothermia was greater, from 48 ± 3 ms (instead of 31 ± 1 prior to bupivacaine) to 107 ± 6 ms ($p < 0.001$). Likewise, ERP increased from 161 ± 4 to 200 ± 3 ms ($p < 0.001$) with the additional influence of hypothermia. The prolongation in ERP was non-significant with bupivacaine alone.

Discussion. Although 4 - 6° C of hypothermia does not markedly impair ventricular conduction (2), this degree of hypothermia will potentiate the adverse effects of bupivacaine. Potentiation is not dependent on a significant rise in bupivacaine plasma concentrations as long as hypothermia does not exceed 3° C. Bupivacaine levels rose above 3.5 µg/ml only at 35° C, when blood pressure was decreased by more than 30 mmHg, with probable reduction in bupivacaine clearance.

We impute this effect of hypothermia to a reduction in cellular oxidative processes which provide energy for the ionic pump mechanisms (i.e., a 50 % reduction in oxygen consumption for a 10° C fall in core temperature), thereby leading to decreased polarization of ventricular contractile fibers. This decrease is much more detrimental to conduction in the presence of bupivacaine, which tends to simultaneously block fast sodium channels.

Consequently, every fall in core temperature is to be avoided during locoregional anesthesia with bupivacaine.

References

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