EFFECTS OF HYPO- AND HYPERNATREMIA ON THE DEPRESSION OF VENTRICULAR CONDUCTION AND ARRHYTHMIAS INDUCED BY BUPIVACAINE

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Introduction. Significant decreases in plasma sodium levels have been reported following transurethral resection of the prostate, as a result of hemodilution caused by systemic absorption of substantial volumes of hypotonic solutions (1.5 % glycine (1), or distilled water) used for bladder irrigation. Hyponatremia also might result from rapid intraoperative i.v. infusion of large amounts of hypotonic glucose. The aim of this study was to determine whether hyponatremia increases the risk of bupivacaine (Bup) toxicity, since ventricular disturbances caused by Bup depend on blockade of the fast sodium channels (2) which might be enhanced by a reduction in transmembrane sodium gradient. Conversely, hypernatremia, by increasing transmembrane gradient, might alleviate Bup induced cardiac disorders.

Methods. The experiments were performed in 24 dogs anesthetized with thiopental (4 mg/kg) and chloralose (80 mg/kg), artificially ventilated to keep normal arterial blood gas tensions and pH, and warmed to prevent hypothermia. Mean arterial blood pressure and the duration of the QRS complexes were continuously recorded. Conduction time (CT) was determined in the ventricular contractile tissue by means of two endocavitary electrodes, one advanced to the apex, and the other, the pacing electrode, placed near the base. In view of the rate-dependency of conduction disorders, a high pacing rate, i.e. 180/min, was selected. Effective refractory period (ERP) was measured by the extrastimulus method (3).

In group 1 (hyponatremia + bupivacaine ; n = 8) a 4 mg/kg loading dose of Bup was administered i.v., followed by Bup infusion at an average rate of 0.1 mg/kg/min in order to produce a prolongation of CT of more than 50 %. The Bup concentrations necessary for this (determined by HPLC) were between 2 and 3.5 µg/ml. After maintaining a steady state for 50 - 60 min, hyponatremia was produced by i.v. infusion of hypotonic (1.5 %) glycine solution, 10 ml/kg/min, over 5 min. In group 2 (hypernatremia + bupivacaine ; n = 8), dogs received Bup according to the same protocol as in group 1, and then were rendered hypernatremic by injection of hypertonic molar sodium lactate solution, 10 ml/kg. In group 3 (hyponatremia alone ; n = 8), dogs received no bupivacaine, but were rendered hyponatremic by infusion of twice the amount of glycine solution as was given in group 1.

Statistical analyses were performed using a Student's t test for paired values between values observed under hypo- or hypernatremia added to Bup and values under Bup alone (group 1 and 2) and between values observed under hyponatremia and control values (group 3).

Results.

Group 1 : Induction of hyponatremia (a decrease in serum sodium from 147 ± 1 (mean ± SEM) to 116 ± 3 mmol/l) ($p < 0.001$), considerably aggravated the disorders induced by Bup, particularly the slowing of conduction. Duration of the QRS complexes was prolonged from 75 ± 6 to 95 ± 8 ms ($p < 0.001$), CT from 55 ± 5 to 77 ± 6 ms ($p < 0.01$), and ERP from 170 ± 8 to 191 ± 11 ms ($p < 0.05$). These changes were not correlated with a reduction of osmolality (which changed only minimally from 308 ± 3 to 291 ± 4 mOsm/kg) but were correlated with serum sodium levels. All parameters returned towards control values within 15 - 30 min of terminating the hyponatremic state. Ectopic beats, wave burst arrhythmia, and even fibrillation occurred each time conduction was severely depressed.

Group 2 : Hypernatremia (serum sodium 168 ± 4 mmol/l) ($p < 0.01$) partially antagonized the disturbances induced by Bup (e.g. CT decreased from 53 ± 2 to 42 ± 3 ms), but differences did not reach statistical significance.

Group 3 : Hyponatremia alone, to the same degree as in group 1, did not produce statistically significant changes. However, more severe hyponatremia (serum sodium 100 - 110 mmol/l) resulted in abnormalities similar to those caused by moderate hyponatremia and Bup (group 1).

Discussion. Reduction of serum sodium to between 120 and 115 mmol/l (i.e. levels seen in the clinical setting) is sufficient to enhance the depressant effects of Bup on ventricular conduction. Reduction of transmembrane gradient and polarization by hyponatremia could conceivably exacerbate the severity of disturbances induced by Bup, the action of which is to diminish sodium conductance (2). These effects predominate at high heart rates, perhaps because sodium extrusion by the pump mechanisms is compromised by the short duration of diastole.

Peridural anesthesia with Bup is not recommended in transurethral resection of the prostate if this operation is accompanied by a bladder irrigation with considerable amounts of hypotonic solutions.

References

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