Title: CARDIOVASCULAR EFFECTS OF VERAPAMIL DURING ACUTE HYPERKALEMIA AND AFTER CALCIUM THERAPY

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Introduction. Verapamil inhibits slow inward calcium currents across excitable membranes. The drug has recently been approved by the FDA for supraventricular tachyarrhythmias and increasing numbers of cardiac surgical patients are now receiving Ca++ channel blockers. Either hyperkalemia or verapamil can result in second-degree atrioventricular (AV) block.1 Verapamil and hyperkalemia both can depress myocardial contractility.1 Clinically, hyperkalemia is possible after massive transfusion, intravenous potassium infusion, or excessive potassium cardioplegia. Calcium is standard initial therapy for hyperkalemia. We studied hemodynamic and electrocardiographic effects of verapamil pretreatment on acutely hyperkalemic dogs. We also evaluated effectiveness of calcium therapy for acute hyperkalemia after verapamil pretreatment.

Methods. Two studies separated by at least one week were done on each of 7 mongrel dogs anesthetized with 1 MAC halothane and treated with IV KCl at a rate of 0.075 meq/kg-min. During one study in each dog, verapamil 0.15 mg/kg bolus plus an infusion of 5.6 µg/kg/min was given 10 minutes prior to beginning the KCl infusion, but no verapamil was given in the other study on each animal. The 2 studies in each dog were done in random order. KCl was infused until ECG changes typical of severe hyperkalemia or AV block occurred. At that point, CaCl₂, 14 mg/kg bolus was given. Hemodynamics were monitored throughout the K+ infusion and after CaCl₂ administration, as were serum K+, whole blood ionized Ca++, and blood gases. Serum K+ and hemodynamics were measured just prior to Ca++ therapy, and at 1, 3, 5, 15, and 30 min thereafter. KCl was stopped when Ca++ was given. Statistics were by paired Student's 't' test with P<0.05 considered significant.

Results. Verapamil in the presence of severe hyperkalemia (K+>5.4±0.2 meq/l without verapamil and 8.8±0.8 with verapamil) resulted in lower CI's, namely 3.0±0.2 l/min-m² without verapamil vs 1.3±0.5 with verapamil pretreatment. Average MAP's were numerically but not significantly lower in hyperkalemic dogs pretreated with verapamil (96±5 vs 96±7 without verapamil). CaCl₂ treatment improved hemodynamics of verapamil pretreated dogs toward but not to that seen after CaCl₂ treatment for hyperkalemia in dogs not pretreated. All verapamil treated hyperkalemic dogs vs none without verapamil had persistent AV block 1 min after Ca++ bolus.

Total meq of KCl infused at the same rate into verapamil pretreated dogs required to produce similar serum potassium levels was one third that required in dogs not verapamil pretreated. (1.6±0.3 meq/kg vs 5.4±0.73 meq/kg).

Discussion. Halothane anesthetized dogs rendered acutely hyperkalemic to similar serum levels of K+ poorly tolerated this level of hyperkalemia when pretreated with verapamil vs non-pretreated hyperkalemic controls. More AV block was seen in the verapamil-hyperkalemic group after Ca++ therapy. The fact that calcium resulted in improved hemodynamics despite persistent AV block implies direct myocardial depression in addition to impaired AV conduction by the combination of verapamil and hyperkalemia. Ca++ only partially reversed the hemodynamic consequences of verapamil plus hyperkalemia. Clinically, hyperkalemia may be poorly tolerated in the presence of verapamil. Calcium treatment for hyperkalemia, when verapamil is present, remains partially effective for hemodynamic depression, but not AV block. The latter agrees with Hariman et al2 who reported that Ca++ reverses hemodynamic depression but not AV conduction defects due to large doses of verapamil in the normokalemic dog. Two previous studies have examined the combination of hyperkalemia after verapamil. The fact that only one third as much KCl resulted in a similar level of serum K+ after verapamil indicates that compensatory mechanisms for controlling extracellular K+ may be impaired by verapamil. We conclude that Ca++ is still therapeutic for acute hyperkalemia in the presence of verapamil but that the Ca++ channel blocker may a result in more severe hemodynamic depression with hyperkalemia; b) be associated with more frequent AV block after treatment with calcium; c) render hyperkalemia likely after considerably less Ca++ administration.

References.