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

Authors: M. Nugent, M.D., J. H. Tinker, M.D.

Affiliation: Department of Anesthesiology, Mayo Clinic and Mayo Medical School, Rochester, MN 55905.
Supported in part by GM24531 from NIH (Dr. Tinker).

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.[1,2] Verapamil and hyperkalemia both can depress myocardial contractility.[1,3] 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 .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 two 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, $CaCl_2$, 14 mg/kg bolus was given. Hemodynamics were monitored throughout the K+ infusion and after $CaCl_2$ 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 $P<.05$ considered significant.

Results. Verapamil in the presence of severe hyperkalemia (K+=9.4±0.2 meq/l without verapamil and 8.2±0.8 with verapamil) resulted in lower CI's, namely 3.0±0.2 l/min·m^2 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 (60±13 vs 96±7 without verapamil). $CaCl_2$ treatment improved hemodynamics of verapamil pretreated dogs toward but not to that seen after $CaCl_2$ 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 5.0±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 al[2] who reported that Ca++ reverses hemodynamic depression but not AV conduction defects due to large doses of verapamil in the normokalemic dog. No 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 K+ administration.

	Serum K+ meq/l		HR (BPM)		MAP (mmHg)		CI l/min·m^2		Number of Dogs with AV Block*	
	Group I	Group II	Group I	Group II	Group I	Group II	Group I	Group II	Group I	Group II
Control	3.3±0.1	3.5±0.3	140±10	116±10	97±9	94±13	4.2±0.5	3.7±0.5	0	0
Post Verapamil	-	3.3±0.2	-	124±9	-	85±9	-	4.1±0.5	-	0
Prior to Ca++ Therapy	9.4±0.2	8.2±0.8	106±9	122±18	96±7	60±13	3.0±0.2*	1.3±0.5*	3	3
1 minute Post Ca++ Therapy	9.3±0.2	8.9±1.9	180±19	78±24	110±13	66±7	4.2±0.4*	2.4±0.4*	0*	5*

Group I - Hyperkalemia
Group II - Verapamil and Hyperkalemia

N = 5, mean±SEM
* Significant difference between Group I and Group II

References.

1. Fisch C: Relation of electrolyte disturbances to cardiac arrhythmias. Circulation 47:408-419, 1973
2. Hariman RJ, Mangiardi LM, McAllister RG, et al: Reversal of the cardiovascular effects of verapamil by calcium and sodium: Differences between electrophysiologic and hemodynamic responses. Circulation 59:797-804, 1979.
3. Surawicz B, Chlebus H, Mazzoleni A, et al: Hemodynamic and electrocardiographic effects of hyperpotassemia. Differences in response to slow and rapid increases in concentration of plasma K. Am Heart J 73:647-664, 1967.