

TITLE: CALCIUM KINETICS AFTER BOLUS INJECTION OF CALCIUM CHLORIDE prior to and during cardiopulmonary bypass

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I. Introduction

Calcium chloride (CaCl<sub>2</sub>) is a commonly used inotrope with a rapid onset but limited duration of hemodynamic effect (15-30 minutes). (1,2) The objectives of our study were (1) to determine the kinetics of ionized calcium (Ca<sup>+2</sup>), the active moiety, and total calcium (Ca<sub>t</sub>) following bolus injections of CaCl<sub>2</sub> in steady states prior to and during cardiopulmonary bypass (CPB) and (2) to determine the effect on the levels of Ca<sup>+2</sup> and Ca<sub>t</sub> of the hemodilution associated with the institution of CPB when a clear prime is used. This study was approved by our institutional Committee on Human Experimentation.

II. Methods

Fifty-four patients undergoing open heart surgery were studied and divided into 3 groups. In Group I (6 patients) Ca<sup>+2</sup> and Ca<sub>t</sub> values were determined at the start of CPB and at 2, 4, 8, 15, 30 and 60 minutes. In Group II the same values were determined in four subgroups of six patients each at 0, 1, 2, 4, 5, 10, 20, and 40 minutes after injection of 0, 2.5, 5, or 10 mg/kg CaCl<sub>2</sub> after 30 minutes of CPB. In Group III for 4 subgroups of six each the same measurements were made as in Group II except that the bolus injections were made 60 minutes prior to the commencement of CPB.

III. Results

The tables for the three groups demonstrate that bolus injections of CaCl<sub>2</sub> produce a marked, but transient, rise in Ca<sup>+2</sup>. The effect of such injections on Ca<sub>t</sub> is less pronounced and even more transient. Hemodilution associated with CPB produces a significant decrease in Ca<sup>+2</sup> and Ca<sub>t</sub>, the effect being more pronounced and lasting longer with respect to Ca<sub>t</sub>.

Group I. Changes in Ca<sup>+2</sup> and Ca<sub>t</sub> with CPB Hemodilution

No CaCl<sub>2</sub> injection, means of 6 subjects

Minutes of Cardiopulmonary Bypass

Calcium	zero	2	4	8	15	30	60
Ionized	2.02	1.63*	1.73*	1.76*	1.81*	1.85*	1.80*
Total	8.12	6.69*	6.72*	6.64*	6.95*	6.93*	6.76*

Group II. Ca<sup>+2</sup> and Ca<sub>t</sub> after bolus CaCl<sub>2</sub> during CPB

Means of 6 subjects in each subgroup

Injection (mg/kg)	Time following injection (in minutes)								
		zero	1	2	4	5	10	20	40
Zero	Ion	1.94	1.96	1.98	2.02	1.95	1.96	1.98	2.02
	Tot	2.09	7.41	7.45	7.42	7.40	7.12	7.29	7.11
2.5	Ion	2.00	2.34*	2.39*	2.22*	2.20*	2.18*	2.17*	2.20*
	Tot	7.43	9.04*	8.71	8.04	8.03	7.83	7.68	7.61
5.0	Ion	1.75	2.48*	2.42*	2.27*	2.26*	2.15*	2.07*	2.04*
	Tot	7.48	10.20*	10.10	9.54	9.50	8.96	8.52	7.97
10.0	Ion	1.86	2.30*	2.33*	2.33*	2.76*	2.18*	2.08*	2.13*
	Tot	7.74	8.91*	9.11	8.77	8.88	8.55	8.02	7.97

Group III. Ca<sup>+2</sup> and Ca<sub>t</sub> after bolus CaCl<sub>2</sub> before CPB

Means of 6 subjects in each subgroup

Injection (mg/kg)									
		Zero	Ion	2.18	2.20	2.20	2.16	2.14	2.16
Zero	Tot	8.34	8.44	8.42	8.39	8.42	8.21	8.12	8.11
	2.5	Ion	2.23	2.56*	2.49*	2.42*	2.40*	2.36*	2.34*
2.5	Tot	8.30	9.57*	9.11*	8.94*	9.00*	8.92*	8.69*	8.62*
	5.0	Ion	1.96	2.76*	2.59*	2.51*	2.49*	2.38*	2.32*
5.0	Tot	8.43	10.59*	10.08*	9.57*	9.60*	9.16*	9.10*	8.85*
	10.0	Ion	2.14	3.53*	3.06*	2.93*	2.87*	2.66*	2.55*
10.0	Tot	8.51	13.03*	11.82*	11.32*	10.94*	10.08*	9.95*	9.44*

\* = Value significantly different from zero while,

----- P < 0.005, paired T-test -----

IV. Discussion

During initiation of CPB with a clear prime and the resultant hemodilution, the drop in Ca<sup>+2</sup> value is mild and transient while the decrease in Ca<sub>t</sub> is greater and more persistent. This indicates that there will often be a need for CaCl<sub>2</sub> injection at the termination of CPB.

Ca<sup>+2</sup> is rapidly bound to citrate, lactate, sulfate or protein. (3) However, even 40 minutes post-injection a significant elevation of Ca<sup>+2</sup> persists. There is a rapid fall in Ca<sup>+2</sup> following the increased level seen with bolus injections, the rate of fall towards baseline being direction proportional to the dose (in mg/kg) used. For this reason repeated doses of CaCl<sub>2</sub> may be indicated if the first injection has beneficial, though transient, effects. However, a significant increase in Ca<sup>+2</sup> above the baseline value may persist for up to forty minutes even after 2.5 mg/kg doses of CaCl<sub>2</sub>. This raises the possibility of hypercalcemia and digitalis toxicity with repeated doses. During our single bolus study a transient bradycardia (pulse=40) was noted on one occasion immediately following injection. Thus, we suggest that while repeated boluses of CaCl<sub>2</sub> may be indicated so long as beneficial hemodynamic effects are observed, the risk of hypercalcemia must be kept in mind and doses not repeated without Ca<sup>+2</sup> measurements if previous doses have had no beneficial hemodynamic effect.

1. Denlinger JR et al: Cardiovascular responses to calcium administered intravenously to man during halothane anesthesia. Anesthesiology 42:390-397, 1975.
2. Hug CC, Kaplan JA: Pharmacology-cardiac drugs in cardiac anesthesia. JA Kaplan Editor, Grune and Stratton 1st Edition, pg 60.
3. Moore EW: Ionized calcium in normal serum, ultrafiltrates and whole blood determined by ion-exchange electrodes. J Clin Invest 49:318-334, 1970.