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TITLE: CONTINUOUS IN VIVO MONITORING OF IONIZED CALCIUM USING ISFET'S

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Introduction. We have used Ca^{++} ISFET (Ion Selective Field Effect Transistor) probes to continuously monitor changes in ionized calcium activity in blood during sodium citrate infusion in dogs. Cardiovascular system performance was also monitored. We have further tested the Ca^{++} ISFET probe as a control sensor for use in controlling Ca^{++} activity by infusion of sodium citrate or calcium chloride to maintain Ca^{++} activity in venous blood at desired values.

Method. Sodium citrate infusion - Eight 20 kg mongrel dogs were studied. Anesthesia was induced with 25 mg/kg thiopental. The animals were then intubated and ventilated using oxygen. Anesthesia was maintained with 1.5% inspired halothane concentration. Arterial pressure monitoring and periodic arterial serum samples were obtained from an arterial line introduced via the right femoral artery. Arterial serum sample Ca^{++} activities were determined using an ion selective electrode instrument (AMT Clin-Ion, Applied Medical Technology, Palo Alto, CA). A Swan-Ganz catheter provided cardiac output, pulmonary artery and wedge pressures. The precalibrated Ca^{++} ISFET probe was introduced via the left jugular vein and was advanced to the region of the right atrium. Three sodium citrate doses were infused. Each infusion was 30 ml in volume and was infused over a 6 min period. Sodium citrate concentrations were selected to simulate infusion of 1, 2 and 4 units of CPD blood in a 70 kg patient: 1) 24 mg/kg, 2) 48 mg/kg and 3) 96 mg/kg sodium citrate. Time for recovery to control conditions was permitted between infusions.

Ca^{++} control experiment - As an extension of continuous in vivo monitoring of Ca^{++} in blood, the concept of feedback control of Ca^{++} was investigated. An experiment preparation similar to that of the citrate infusion study was used. In this experiment, however, the Ca^{++} ISFET probe was positioned in the inferior vena cava. Ca^{++} activity in venous blood returning from the abdominal organs and lower extremities was monitored. Hypocalcemia was produced after an initial 30 min stabilization period by infusing sodium citrate (100 mg/ml in deionized water) at rates needed to achieve and maintain the desired Ca^{++} activity of 1.0 mEq/L for a period of 30 min. Venous serum Ca^{++} activity of 1.0 mEq/L with inspired halothane concentration of 1.5% was found during previous experiments to be tolerated by dogs for at least 30 minutes. Hypercalcemia (3.0 mEq/L) was then produced by infusing calcium chloride (100 mg/ml USP injectate); infusion rates were adjusted as needed to maintain the desired Ca^{++} activity for an additional 30 minutes. Venous serum Ca^{++} activity of 3.0 mEq/L with inspired halothane concentration of 1.5% was found during previous experiments to be tolerated by dogs.

Ca^{++} ISFET probe description - ISFET sensors have been described previously.[1] The Ca^{++} ISFET probe used in these experiments was identical to the probe design described in ref. 1, but a Ca^{++}-selective membrane replaced the K^{+}-selective membrane. The entire probe was contained in a single 6 French catheter. Precalibration of the Ca^{++} ISFET probes for the citrate infusion experiments was performed by presetting Ca^{++} activity response and temperature compensation gains in vitro using 1.0 and 10.0 mEq/L Ca^{++} standards containing no protein at room temperature and 38° C; mEq/L readout was set to correspond with the baseline arterial serum sample Ca^{++} analysis. Precalibration for subsequent Ca^{++} control experiments including results presented in Fig. 1 was performed using reconstituted lyophilized human sera standards. Accurate mEq/L ISFET Ca^{++} readouts were obtained directly thus eliminating reliance on baseline serum sample analysis.

Results. Sodium citrate infusion - Changes in ISFET Ca^{++} data (averages $\pm$ standard errors) for the 8 animals studied are presented in Table 1 with cardiac output and mean arterial pressure changes.

Ca^{++} control experiment - Results of the experiment during which Ca^{++} activity in venous blood was controlled are shown in Fig. 1. Arterial serum sample Ca^{++} analyzed using an ion selective electrode instrument (AMT Clin-Ion) are indicated by open circles. The discrepancy between the Ca^{++} ISFET reading and the 1.5 hr arterial serum sample value during $CaCl_2$ infusion is probably attributable to the difference between the Ca^{++} ISFET sensor location (IVC) and the arterial sample site (abdominal aorta).

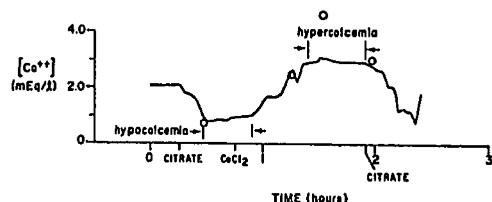
Reference.

1. McKinley BA, Saffle J, Jordan WS, et al: In vivo continuous monitoring of K^{+} in animals using ISFET's. Medical Instrumentation 14:93-97, 1980

Table 1.

	ISFET Ca^{++} (mEq/L)	CO (l/min)	MAP (mm Hg)
Range Control	(0.50-2.41)	(0.78-3.56)	(58-107)
Dose (6 min)	100%	100%	100%
24 mg/kg	70.0 $\pm$ 7.3%	89.5 $\pm$ 6.0%	99.7 $\pm$ 2.8
48 mg/kg	67.1 $\pm$ 6.6	92.5 $\pm$ 6.0	95.3 $\pm$ 0.2
96 mg/kg	53.9 $\pm$ 13.0	67.8 $\pm$ 18.2	79.5 $\pm$ 9.7

Figure 1. Ca^{++} ISFET Recording



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