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Serum Potassium, Calcium and Magnesium After Resuscitation From Ventricular Fibrillation: A Canine Study

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Serum electrolytes were measured before and sequentially for 3 hours after resuscitation from ventricular fibrillation in a canine model that was designed to approximate the human cardiac arrest and resuscitation process. Twenty anesthetized dogs were resuscitated from ventricular fibrillation; 7 required epinephrine during resuscitation and 13 did not. To control for the effects of anesthesia, 10 dogs were anesthetized and instrumented, but ventricular fibrillation was not induced.

Serum potassium decreased from 3.7 ± 0.3 mmol/liter at baseline to 3.2 ± 0.4 mmol/liter 45 minutes after resuscitation in the experimental dogs resuscitated without epinephrine, as compared with 3.6 ± 0.3 to 3.4 ± 0.2 mmol/liter in control dogs ($p = 0.07$ versus control dogs by two-way analysis of variance) and returned toward baseline at the end of 3 hours. Serum calcium decreased from 9.6 ± 0.6 mg/dl at baseline to 8.9 ± 0.9 mg/dl at 5 minutes after resuscitation as compared with 9.4 ± 0.7 to 9.5 ± 0.7 mg/dl in control dogs ($p < 0.05$ versus control dogs) and returned to baseline by 3 hours. Serum magnesium decreased from 1.5 ± 0.1 to 1.3 ± 0.2 mEq/dl by 3 hours in resuscitated dogs as compared with 1.6 ± 0.2 to 1.5 ± 0.2 mEq/dl in control dogs ($p = 0.06$ versus control dogs). These changes in serum potassium, calcium and magnesium were independent of the administration of epinephrine during the resuscitation process. Changes in potassium were independent of arterial pH or bicarbonate therapy. Serum glucose increased after ventricular fibrillation but not in control dogs ($p < 0.0005$ versus control). No changes in other electrolytes were observed.

Thus, serum potassium, calcium and magnesium decreased after resuscitation from ventricular fibrillation in this canine model. These data suggest that, although the hypokalemia seen after ventricular fibrillation in humans may in some cases precede the event, a decrease in potassium may develop after resuscitation.

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A high incidence of hypokalemia has been observed in humans after resuscitation from cardiac arrest. When serum potassium was measured immediately after arrival in the emergency room, 49% of 115 resuscitated patients were hypokalemic (potassium <3.5 mEq/liter) in one study (1) and 41% of 138 patients in another study (2); 17 and 11% of the patients had serum potassium levels of <3.0 mEq/liter in the respective studies. In both studies, the frequency of postresuscitation hypokalemia was greater than was found with acute myocardial infarction. Although hypokalemia has also been observed in humans during hospitalization for myocardial infarction and other forms of stress, its incidence appears greatest after resuscitation (3,4).

Hypokalemia is known to increase ventricular ectopic activity including nonsustained ventricular tachycardia (5,6). Patients with hypokalemia after myocardial infarction have an increased incidence of ventricular fibrillation during hospitalization (7,8). Because hypokalemia has been observed to result in an increased incidence of arrhythmia, it is speculated that hypokalemia may have caused some of the episodes of cardiac arrest that occurred outside the hospital in the preceding studies. However, because it is very unusual for patients to have their serum potassium measured immediately before their out-of-hospital event, the true frequency of hypokalemia before cardiac arrest is unknown.

It has been reported (9,10) that the infusion of epinephrine in volunteers consistently results in a decrease in serum potassium of up to 1 mmol/liter. We hypothesized that the stress of ventricular fibrillation or the treatment of ventricular fibrillation might result in a decrease in serum potassium. To test this hypothesis, we observed the response of

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serum potassium to ventricular fibrillation and its resuscitation in a canine model designed to approximate the human cardiac arrest and resuscitation process.

Methods

Study animals. Thirty adult mongrel dogs (average weight 16.5 ± 1.7 kg) were studied. Twenty dogs served as the experimental group that had initiation of and resuscitation from ventricular fibrillation. Ten dogs served as the control group; they underwent all procedures including anesthesia, ventilation, intravenous fluids, catheter placement and 3 hours of blood sampling, but did not undergo ventricular fibrillation or resuscitation. The dogs were all handled in standard fashion and were fed a standard dried dog chow; they were not fed on the morning of the study. Animals were maintained and studies conducted in accordance with the guidelines of the American Association for Accreditation of Laboratory Animal Care (AAALAC). The study protocol was approved by the Animal Care and Use Committee of Hennepin County Medical Center.

Anesthesia/instrumentation. Experimental and control dogs underwent the following procedures. A peripheral intravenous line was established in the foreleg, and diazepam (0.25 mg/kg body weight) was infused. An infusion of normal saline solution was continued at 50 cc/h throughout the study in both experimental and control dogs. The dogs were then anesthesized with ketamine (7 mg/kg) and pancuronium (0.08 mg/kg). Anesthesia was maintained for the duration of the protocol, using intravenous injections of one-fourth of the initial dose of anesthetic agent (ketamine plus pancuronium) as required.

The dogs were intubated by the oral-tracheal route under direct visualization. Ventilation was maintained at a tidal volume of 25 cc/kg and a respiratory rate of 12 cycles/min (Harvard volume respirator model 613). Supplemental oxygen (2 liters/min) was used to compensate for dead space in the respiratory apparatus. Baseline arterial partial pressure of oxygen (P_{O_2}) values were only minimally elevated (Table 1).

Using standard cutdown technique, a catheter was placed in the inferior vena cava by way of the femoral vein and located just below the right atrium for infusion of medications during the resuscitation process. Through the other femoral vein, a bipolar pacing electrode was placed in the right ventricle for induction of ventricular fibrillation. A catheter was placed through the femoral artery into the thoracic aorta for obtaining arterial blood gas and serum chemistry values. After placement of these catheters (approximately 30 minutes), baseline arterial blood gas and serum laboratory data were obtained.

Ventricular fibrillation/resuscitation protocol. The resuscitation protocol in this experiment was designed to approximate typical metropolitan two-tiered emergency response systems for out-of-hospital cardiac arrest (11). In these systems, emergencies are first responded to by emergency medical technicians who initiate basic cardiopulmonary resuscitation with closed chest massage and assist ventilation with supplemental oxygen. Paramedic teams then arrive at the scene and administer advanced life support with electrical defibrillation and intravenous medications.

The following procedures were performed only in the experimental dogs. Ventricular fibrillation was induced using half-wave rectified alternating current (60 Hz, 17 V peak, 6.7 V root-mean-square) directed through the pacing electrodes to the right ventricle. Ventricular fibrillation was untreated for a mean of 1.1 minutes (range 0.5 to 2), to simulate the time to arrival of emergency medical technicians in cardiac arrest in humans. During this period, the dogs were removed from the ventilator and no cardiopulmonary resuscitation was performed. After this initial period, positive pressure ventilation was resumed with an increase in respiratory rate to 20 cycles/min and an increase in oxygen flow from 2 liters/min to 10 liters/min. Closed chest cardiac massage using lower thoracic two-sided lateral compressions was performed at a rate of approximately 120 beats/min. This rate is higher than that used in humans, but more closely simulates the normal canine heart rate. Cardiopulmonary resuscitation was continued in this fashion for an average of 1 minute (range 0.5 to 2) to simulate the time delay from arrival of emergency medical technicians to arrival of the paramedic units in cases of human cardiac arrest. Thus, total ventricular fibrillation time before attempted defibrillation was 2 minutes (range 1 to 4). After these procedures, direct current defibrillation was performed using 100 watt-seconds as initial current. If the initial shock failed to convert the ventricular fibrillation, 200 watt-seconds were delivered.

Medications were then administered according to the paramedic protocol in effect at the time we and others made the clinical observations that stimulated this experiment (1,2). The following medications were administered as indicated during resuscitation. Epinephrine (0.014 mg/kg) was given for ventricular fibrillation that was not cardioverted by two direct current shocks, for pulseless idioventricular rhythm and for asystole. Bicarbonate (0.2 to 0.7 mEq/kg) was given for ventricular fibrillation if cardioversion was not successful, for hypotensive bradycardia including asystole and during prolonged resuscitation efforts. Lidocaine (2 mg/kg) was given for ventricular tachycardia, for ventricular fibrillation not controlled by cardioversion and epinephrine and for frequent ventricular beats. Calcium (0.14 mg/kg) was given for asystole. Atropine (0.2 mg) was given for bradycardia, particularly with atrioventricular (AV) block. The oxygen settings were decreased to 2 liters/min and the respiratory rate was decreased to 12 cycles/min 15 minutes after initial defibrillation.

Laboratory data. Laboratory data were collected in both experimental and control dogs at baseline and 5, 15, 30,

Table 1. Electrolytes and Arterial Blood Gases After Ventricular Fibrillation

	No. of Dogs	Baseline	5 min	15 min	30 min	45 min	60 min	90 min	120 min	180 min	p Value (ANOVA)
Potassium (mmol/liter)											
Control	10	3.6 ± 0.3	3.6 ± 0.2	3.4 ± 0.2	3.4 ± 0.2	3.4 ± 0.2	3.3 ± 0.3	3.5 ± 0.3	3.6 ± 0.2	3.6 ± 0.2	0.08
VF, total	20	3.7 ± 0.3	4.2 ± 0.8	4.0 ± 1.2	3.3 ± 0.4	3.2 ± 0.4	3.2 ± 0.4	3.3 ± 0.4	3.4 ± 0.3	3.5 ± 0.3	<0.00001
VF, epi	7	3.8 ± 0.4	5.0 ± 0.8	4.8 ± 1.7	3.5 ± 0.4	3.3 ± 0.6	3.1 ± 0.4	3.3 ± 0.4	3.6 ± 0.2	—	<0.01
VF, no epi	13	3.7 ± 0.3	3.9 ± 0.6	3.5 ± 0.2	3.3 ± 0.3	3.2 ± 0.3	3.2 ± 0.4	3.3 ± 0.4	3.4 ± 0.3	3.5 ± 0.3	<0.00001
"Corrected" potassium (mmol/liter)											
Control	10	3.6 ± 0.3	3.6 ± 0.3	3.4 ± 0.2	3.4 ± 0.2	3.4 ± 0.2	3.3 ± 0.2	3.5 ± 0.3	3.6 ± 0.2	3.5 ± 0.3	0.15
VF, no epi	13	3.6 ± 0.3	3.8 ± 0.6	3.4 ± 0.2	3.2 ± 0.3	3.1 ± 0.3	3.1 ± 0.4	3.2 ± 0.3	3.3 ± 0.3	3.5 ± 0.3	<0.0001
Calcium (mg/dl)											
Control	10	9.4 ± 0.7	9.5 ± 0.7	9.3 ± 0.7	9.4 ± 0.7	9.5 ± 0.6	9.6 ± 0.7	9.6 ± 0.7	9.8 ± 0.7	9.7 ± 0.5	NS
VF, total	17	9.6 ± 0.5	8.8 ± 0.6	8.8 ± 0.8	8.9 ± 0.9	9.0 ± 0.8	9.0 ± 0.9	9.4 ± 0.8	9.5 ± 0.6	9.5 ± 0.6	<0.01
VF, no epi	13	9.6 ± 0.6	8.9 ± 0.6	8.9 ± 0.7	9.1 ± 0.7	9.2 ± 0.7	9.2 ± 0.9	9.5 ± 0.8	9.5 ± 0.7	9.5 ± 0.6	0.11
Magnesium (mEq/dl)											
Control	10	1.6 ± 0.2	1.6 ± 0.2	1.6 ± 0.2	1.6 ± 0.2	1.6 ± 0.2	1.6 ± 0.2	1.6 ± 0.2	1.6 ± 0.2	1.5 ± 0.2	NS
VF, total	20	1.5 ± 0.2	1.6 ± 0.2	1.5 ± 0.2	1.5 ± 0.2	1.4 ± 0.2	1.4 ± 0.2	1.4 ± 0.2	1.4 ± 0.2	1.4 ± 0.2	<0.05
VF, no epi	13	1.5 ± 0.1	1.6 ± 0.2	1.5 ± 0.2	1.5 ± 0.2	1.4 ± 0.2	1.4 ± 0.2	1.4 ± 0.2	1.4 ± 0.2	1.3 ± 0.2	0.08
pH											
Control	10	7.42 ± 0.07	7.40 ± 0.06	7.39 ± 0.06	7.38 ± 0.07	7.38 ± 0.07	7.38 ± 0.07	7.36 ± 0.08	7.36 ± 0.08	7.37 ± 0.08	NS
VF, no epi	13	7.31 ± 0.07	7.30 ± 0.09	7.28 ± 0.09	7.29 ± 0.08	7.29 ± 0.06	7.30 ± 0.05	7.32 ± 0.05	7.31 ± 0.06	7.33 ± 0.06	NS
P_{CO_2} (mm Hg)											
Control	10	31 ± 8	32 ± 5	32 ± 6	32 ± 5	32 ± 6	32 ± 5	32 ± 5	32 ± 5	31 ± 5	NS
VF, no epi	13	43 ± 12	39 ± 18	42 ± 17	42 ± 13	42 ± 8	39 ± 6	39 ± 6	39 ± 6	37 ± 6	NS
P_{O_2} (mm Hg)											
Control	10	115 ± 25	112 ± 20	116 ± 22	115 ± 25	113 ± 23	117 ± 25	121 ± 33	115 ± 23	113 ± 22	NS
VF, no epi	13	135 ± 14	231 ± 57	128 ± 44	129 ± 26	140 ± 61	133 ± 50	140 ± 63	161 ± 85	152 ± 68	<0.001
Glucose (mg/dl)											
Control	10	120 ± 25	119 ± 22	122 ± 18	128 ± 17	131 ± 16	140 ± 17	118 ± 25	129 ± 21	133 ± 26	NS
VF, no epi	13	124 ± 17	218 ± 48	191 ± 48	181 ± 51	179 ± 47	176 ± 60	168 ± 45	157 ± 61	131 ± 26	<0.001
VF, epi	7	122 ± 33	245 ± 63	300 ± 127	266 ± 114	221 ± 80	247 ± 82	209 ± 73	201 ± 78	175 ± 70	0.11
Phosphorus (mg/dl)											
Control	10	3.0 ± 1.5	3.0 ± 1.5	2.9 ± 1.5	2.9 ± 1.5	2.8 ± 1.6	3.1 ± 1.5	3.2 ± 1.8	3.4 ± 1.8	4.0 ± 1.8	NS
VF, no epi	13	4.5 ± 1.6	5.0 ± 1.9	4.8 ± 1.9	4.4 ± 1.9	4.7 ± 2.2	4.1 ± 1.8	4.3 ± 2.0	4.8 ± 2.0	5.7 ± 1.9	NS
Sodium (mmol/liter)											
Control	10	148 ± 4	148 ± 3	148 ± 3	148 ± 3	148 ± 3	149 ± 3	149 ± 2	149 ± 3	149 ± 2	NS
VF, no epi	13	145 ± 2	144 ± 3	146 ± 3	147 ± 5	146 ± 3	145 ± 4	146 ± 4	146 ± 3	147 ± 3	NS
Chloride (mmol/liter)											
Control	10	114 ± 6	114 ± 6	115 ± 5	114 ± 7	115 ± 4	116 ± 6	116 ± 5	116 ± 5	116 ± 4	NS
VF, no epi	13	112 ± 5	111 ± 6	113 ± 3	113 ± 5	114 ± 4	112 ± 7	117 ± 10	113 ± 4	113 ± 4	NS

The mean ± SD is shown for early laboratory measurement at baseline just before induction of ventricular fibrillation (VF) and at each time interval after resuscitation. Control dogs were maintained under anesthesia without induction of ventricular fibrillation. Dogs with ventricular fibrillation were subdivided into those that required epinephrine (epi) during resuscitation and those that did not (no epi). p values were derived by one way analysis of variance for repeated measures (ANOVA). "Corrected" potassium (K) was adjusted for arterial pH by the following formula: corrected K = measured K + (pH − 7.4).

45, 60, 90, 120 and 180 minutes after defibrillation. Arterial blood was obtained for pH, partial pressure of carbon dioxide (P_{CO_2}) and P_{O_2} analysis. Serum was obtained for glucose, potassium, calcium, magnesium, phosphorus, sodium and chloride determination. Potassium was analyzed by flame photometry with an internal lithium standard (linearity 2.2 to 10.0 mEq/liter, normal range 3.7 to 5.3 mmol/liter). Magnesium was analyzed by colorimetry with Calmagite, using polyvinyl pyrrolidone and 9-ethyleneoxide to prevent spectrum shift by serum protein and ethylene glycol-bis(β-aminoethylether)-N,N′-tetraacetic acid (EGTA) to prevent calcium interference (linearity 1.0 to 4.0 mEq/liter, normal range 1.3 to 2.6). Calcium was analyzed by colorimetry using o-cresolphthalein (linearity 3.0 to 13.0 mg/dl, normal range 8.1 to 11.3).

The baseline data were compiled for the 30 dogs (experimental plus control groups) in this study. Drawn after 30 minutes of anesthesia, these values represent the "normal" values for anesthetized dogs using our laboratory methods. The baseline levels (mean ± SD) were 3.7 ± 0.3 mmol/liter for serum potassium, 9.5 ± 0.6 mg/dl for calcium and 1.5 ± 0.2 mEq/dl for magnesium. There were no differences in these baseline values between experimental dogs and anesthetized control dogs.

Laboratory analysis. Serum potassium was corrected for pH using the following formula: Kc = Ko + (pH − 7.4), where Kc = corrected potassium, Ko = observed potassium and pH = observed pH. This formula represents the average shift in potassium seen in numerous studies of metabolic acidosis and mild respiratory acidosis, as tabulated in a recent review (12). The traditional formula for the adjustment of serum potassium to pH [Kc = Ko + 6 (pH − 7.4)] was derived using inorganic acid infusions (13) and is believed to overestimate the effect of the mild acidosis after cardiac arrest in this study.

Data analysis. Changes in serum values from baseline for control data and experimental data were analyzed by one-way analysis of variance for repeated measures for each variable. Differences between control and experimental data were tested using two-way analysis of variance (one repeated measure and one not) with the Greenhouse Geisser correction. The unpaired *t* test was used to compare the changes in serum potassium from baseline to 45 minutes for experimental versus control dogs.

Results

Twenty dogs were resuscitated from ventricular fibrillation. Seven required epinephrine infusion during the resuscitation process: all received bicarbonate, all received lidocaine, three received calcium and one received atropine. Of the 13 not requiring epinephrine, 12 received lidocaine, 10 received bicarbonate, 5 received atropine and none required calcium. Arterial pH and P_{CO_2} remained stable throughout the period of study (Table 1). Arterial P_{O_2} increased transiently in the resuscitated dogs because of administration of oxygen ($p < 0.001$).

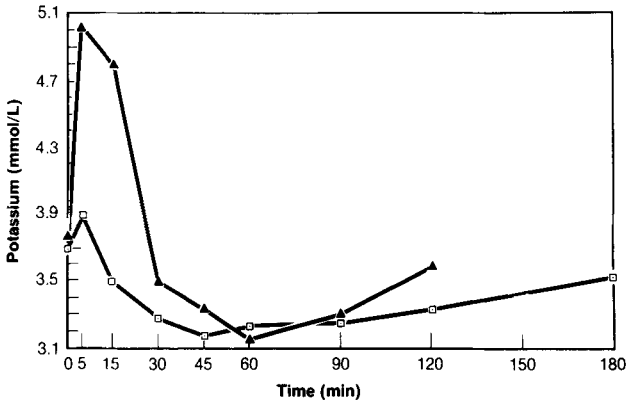
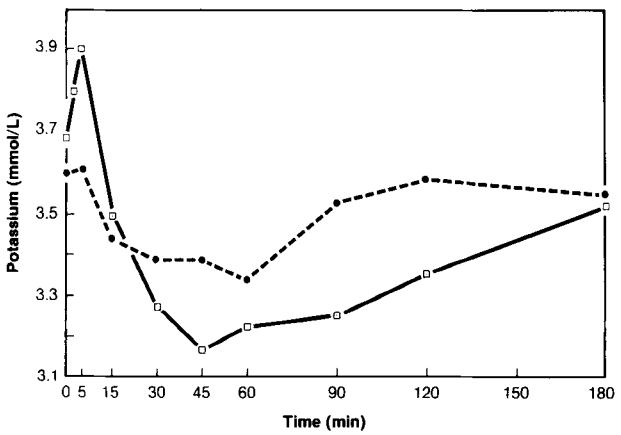


Figure 1. Mean observed serum potassium level for 20 dogs resuscitated from ventricular fibrillation. Dogs were divided into 7 that did (▲) and 13 that did not (⊡) receive exogenous epinephrine. Data are shown for each time interval during the study. See Table 1 for statistical data.

Serum potassium. After resuscitation from ventricular fibrillation, there was a transient increase in serum potassium followed by a decrease that reached its nadir 45 to 60 minutes after fibrillation (Table 1). This pattern was seen whether or not the dogs received epinephrine therapy (Fig. 1). Because of the known effects of epinephrine administration on serum potassium, subsequent comparisons were made between control dogs and those dogs resuscitated without exogenous epinephrine.

A small decrease in serum potassium occurred in the control dogs during the period of study (p = NS by analysis of variance) (Table 1, Fig. 2). A greater decrease in serum

Figure 2. Mean observed serum potassium level for 10 control dogs (●) and 13 dogs resuscitated from ventricular fibrillation without the use of exogenous epinephrine (⊡). These values are shown for each time interval during the study. See Table 1 for statistical analyses.



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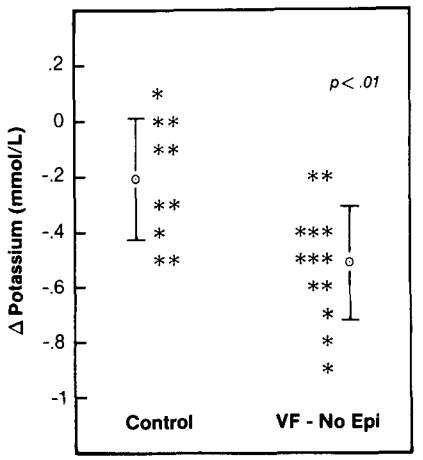
potassium developed after resuscitation from ventricular fibrillation ($p < 0.0001$ versus baseline by analysis of variance and $p = 0.07$ by two-way analysis of variance for dogs resuscitated without epinephrine versus control dogs). The serum potassium reached its lowest value at 45 minutes and was returning toward baseline by 3 hours after ventricular fibrillation. The decrease in potassium was of similar magnitude in dogs treated with epinephrine and dogs not requiring epinephrine. When the serum potassium was adjusted for arterial pH, these changes in serum potassium persisted (Table 1).

The change in serum potassium from its baseline to 45 minutes was calculated for each individual dog. This change was greater in dogs resuscitated from ventricular fibrillation than in control dogs ($p < 0.01$) (Fig. 3). No correlation was found between the duration of ventricular fibrillation and the change in serum potassium from baseline to 45 minutes ($r = 0.08$). Six of the 20 resuscitated dogs had a serum potassium level < 3.0 mmol/liter at some point after resuscitation, whereas 1 of the 10 control dogs had a level <3.0 after the baseline value (p = NS by chi-square analysis).

Effect of medications on serum potassium. The mean change in serum potassium from baseline to 45 minutes was −0.5 mmol/liter for the 13 dogs resuscitated without epinephrine, as compared with −0.4 mmol/liter for the 10 dogs that received epinephrine (p = NS). Three of the dogs received neither epinephrine nor bicarbonate; their mean change in potassium at 45 minutes was −0.6 mmol/liter; this change did not differ significantly from that in the 10 dogs that received bicarbonate but no epinephrine (mean change −0.5 mmol/liter). All but 1 of the 20 dogs received lidocaine, so its effect could not be tested. The change in potassium was −0.5 mmol/liter for the four dogs that received bicarbonate, lidocaine and atropine as compared with −0.5 mmol/liter for the six dogs that received bicarbonate, lidocaine but no atropine (p = NS). Only three dogs (all in the epinephrine group) received calcium therapy; it had no effect on potassium.

Figure 3. Change in the observed serum potassium level from baseline to 45 minutes after ventricular fibrillation (VF) in 13 experimental dogs and from baseline to 45 minutes after the baseline laboratory value in 10 control dogs. Data are shown only for those dogs resuscitated from ventricular fibrillation without the administration of exogenous epinephrine (VF-No Epi). The probability (p) value was derived by unpaired *t* test. (⊙) Mean ± SD.



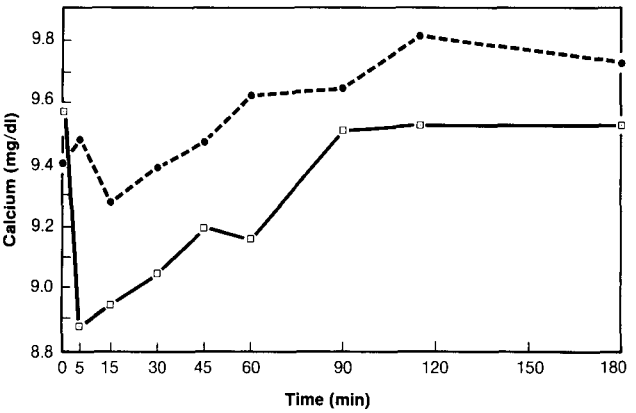


Figure 4. Mean serum calcium level for each time interval during the study. See Table 1 for statistical data. Symbols as in Figure 2.

Serum calcium. The three dogs that received exogenous calcium during resuscitation were excluded from the analysis of serum calcium after resuscitation. Serum calcium decreased after resuscitation from ventricular fibrillation (Fig. 4, Table 1). Its lowest value was seen 5 minutes after resuscitation, and it returned to its prearrest level by 3 hours after resuscitation. No change in calcium was seen in control dogs. The decrease in calcium after ventricular fibrillation was greater in the experimental than in the control dogs ($p < 0.05$ by two-way analysis of variance for dogs resuscitated without epinephrine compared with control dogs). The decrease was seen for both the dogs that received epinephrine and those that did not.

Serum magnesium. Although serum magnesium remained stable in control dogs, a progressive decrease was seen during the first hour after ventricular fibrillation (Table 1, Fig. 5). The lowest value was seen 3 hours after ventricular fibrillation. Serum magnesium was lower in experimental dogs than in control dogs ($p = 0.06$ by two-way analysis of variance for control versus dogs resuscitated without epinephrine). The decrease in serum magnesium after resuscitation occurred both in dogs that received exogenous epinephrine and in those that did not.

Other laboratory data. Serum glucose did not change during the period of study in control dogs but increased both in those dogs requiring epinephrine and in those dogs not treated with epinephrine after ventricular fibrillation (Table 1) ($p < 0.0005$ by two-way analysis of variance for control dogs versus dogs resuscitated without epinephrine). The increase in glucose was greatest in those dogs receiving

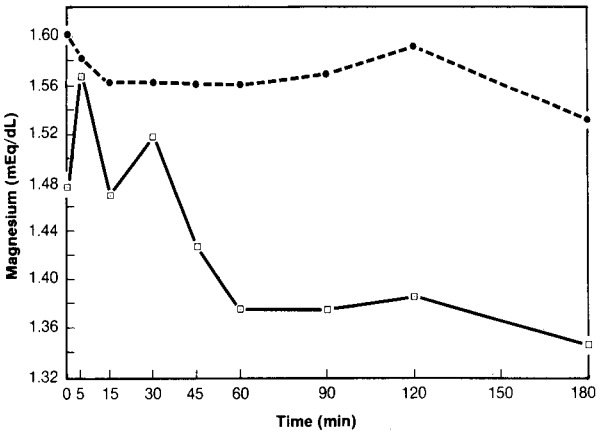


Figure 5. Mean serum magnesium at each time interval during the study. See Table 1 for statistical data. Symbols as in Figure 2.

exogenous epinephrine and reached its peak 5 to 30 minutes after resuscitation. No changes were seen in serum phosphorus, sodium or chloride after resuscitation from ventricular fibrillation, as compared with prearrest baseline values or as compared with control values.

Discussion

Animal model compared with human resuscitation. This canine model was designed to approximate the human cardiac arrest and resuscitation process. It is similar to typical two-stage metropolitan area emergency medical systems for resuscitation of victims of out-of-hospital cardiac arrest (11). In these systems, there is a time delay from initial collapse of the victim to arrival of emergency medical technicians, who then administer basic cardiopulmonary resuscitation while awaiting arrival of a paramedic team who administer advanced life support therapy with electrical cardioversion and intravenous medications. It should be noted that type II statistical errors (failure to detect an important statistical difference) are possible in this study because of the small number of dogs in each group. Nonetheless, significant changes were found in potassium, calcium and magnesium after resuscitation from ventricular fibrillation in these dogs.

The protocol used in this dog study differed in a few ways from the process of cardiac arrest and resuscitation in humans. The major difference was that the dogs were anesthetized for humane purposes. Therefore, an anesthetized control group was used without ventricular fibrillation or resuscitation. This control group underwent otherwise identical procedures including identical intravenous fluid therapy. Ventricular fibrillation and its resuscitation resulted in a statistically greater decrease in serum potassium in the experimental than in the anesthetized control group. Other differences between the human situation and this dog model include administration of low flow supplemental oxygen before the initiation of fibrillation in the dogs to compensate for dead space in the ventilator; this only minimally increased the arterial oxygen saturation. Also, we used a higher chest compression rate in dogs than in humans because of their higher basal heart rate, in an effort to improve the rate of successful resuscitation. This difference should not affect the electrolyte concentrations after resuscitation. The average time from onset of fibrillation to attempted cardioversion was somewhat shorter in the dog model than in humans, to maximize the successful resuscitation rate. Despite this difference, significant changes in electrolytes were found in the dogs. In this dog model, the same drug administration protocol was used as was used in humans at the time the clinical observations were made of frequent hypokalemia after resuscitation from cardiac arrest (1,2). Nonetheless, the decrease in potassium in this study was independent of exogenous epinephrine, bicarbonate, atropine or calcium. Because all but one dog received lidocaine, its effect remains unknown. A final difference between this animal model and humans is that most people resuscitated from cardiac arrest have underlying ischemic heart disease; the effect of this disease on electrolyte changes after resuscitation is unknown.

Postresuscitation hypokalemia. After an initial and brief increase in serum potassium, hypokalemia consistently developed after ventricular fibrillation in these dogs with an average decrease in serum potassium of 0.5 mmol/liter (a 14% decrease). The minimal value for serum potassium was reached 45 minutes after ventricular fibrillation and was returning toward normal by 3 hours after the event. A serum potassium level <3.0 mmol/liter was observed at some point in 30% of the resuscitated dogs. This frequency is comparable with the incidence of hypokalemia observed in resuscitated humans after cardiac arrest (1,2). Thus, although some patients probably sustain ventricular fibrillation as a result of hypokalemia (14), it is possible that the majority of patients who have low serum potassium values shortly after resuscitation develop this finding as a secondary event.

Mechanism of postresuscitation potassium changes. Why do changes in serum potassium occur after ventricular fibrillation? The early increase in potassium may be due to tissue ischemia or the trauma of chest massage, but it is noteworthy that the increase coincides with the increase in serum glucose. Thus, the increase may be due to release of potassium from the liver, possibly mediated by catecholamines. In a canine study (15) of the effects of epinephrine infusion, an early increase in serum potassium was observed, followed by a subsequent decrease in potassium. The subsequent decrease in serum potassium may be caused by a $beta_2$ effect of epinephrine. Although the decrease in serum potassium in this study was independent of exogenous epinephrine administration, the endogenous secretion of

catecholamines was probably large in these dogs. Although we did not measure serum epinephrine levels, high values have been observed in acute medical illnesses (16). In human volunteers, when epinephrine is administered in doses designed to achieve serum levels comparable with those seen during periods of stress, serum potassium has been consistently observed to decrease by 0.5 to 1 mmol/liter (9,10). The effect of epinephrine infusion on serum potassium can be blocked by administration of nonselective or $beta_2$ selective beta-adrenergic blockers but not by $beta_1$-adrenergic blockade (10,17). In subjects pretreated with diuretics to produce hypokalemia, epinephrine infusion further decreases the serum potassium (18). It seems likely that a catecholamine-mediated decrease in potassium might be occurring in this canine model. Support for this speculation is the observation that serum glucose increased consistently in the dogs surviving ventricular fibrillation, presumably as a result of catecholamine secretion. It is possible that catecholamine-induced hypokalemia is mediated by insulin, which is secreted in response to catecholamine-induced hyperglycemia. It is known that insulin augments the cellular uptake of potassium (19).

The cause of the small decrease in serum potassium in the control dogs is unknown. It may have been a result of the stress of anesthesia or an effect of the anesthetic agents used. Although ketamine can decrease serum potassium as a result of release of endogenous catecholamines, this effect is blocked by diazepam, which was administered in this study (20). Because of the effects of anesthesia on sympathetic tone, the exact time of onset and duration of postresuscitation electrolyte changes may differ in nonanesthetized animals and humans.

After its nadir at 45 minutes, the serum potassium level returned toward normal even though no exogenous potassium was administered. Therefore, the decrease in serum potassium in this study was probably caused by a shift in potassium from the intravascular to the extravascular or intracellular space, or both, followed by subsequent return to the intravascular compartment. This observation is compatible with the time course of potassium shifts seen after epinephrine infusion in volunteers. It is believed that epinephrine stimulates a shift of potassium primarily into skeletal muscle cells (21). It is not known whether potassium also enters cardiac muscle cells during epinephrine administration.

Possible effects of postresuscitation hypokalemia. It is also not known what changes occur in the transmembrane electrical potentials in cardiac cells during the hypokalemia that develops after epinephrine administration. Alteration of this transmembrane potential could result in an increased propensity toward arrhythmia. The electrophysiologic effects of catecholamine-induced hypokalemia are unknown. Similarly the electrophysiologic effects of the hypokalemia seen in our dog model are unknown. Postresuscitation hypokalemia may in some cases be due to a shift of potassium into cells. Nonetheless, the hypokalemia observed in humans may have important electrophysiologic consequences during the first 1 to 2 hours after resuscitation from cardiac arrest. It is possible that it increases the likelihood of recurrent arrhythmia during that period. Conversely, the shift of potassium into cells after cardiac arrest may actually be beneficial in maintaining homeostasis, through unrecognized mechanisms.

Potential therapeutic implications of postresuscitation hypokalemia. Nonselective beta-blocker therapy in humans during acute myocardial infarction has been reported to reduce the incidence of both hypokalemia and ventricular arrhythmia, whereas $beta_1$-selective blockers were less effective (22,23). This suggests that the $beta_2$-mediated shift of potassium caused by catecholamines may have a clinically important arrhythmogenic effect. Whether $beta_2$-receptor blockade should be used to treat postresuscitation hypokalemia and potential arrhythmia is unknown.

It is not known whether intravenous potassium should be administered for catecholamine-induced hypokalemia or postresuscitation hypokalemia. Potassium might enter the cellular compartment as rapidly as it is infused, thus potentially further altering the transmembrane electrical potential. Because the serum potassium spontaneously returned toward normal within 3 hours in our canine study, this might also be true in humans. Thus, large amounts of exogenous potassium may result in a rebound hyperkalemia.

Postresuscitation changes in calcium and magnesium. Our observations of a rapid decrease in serum calcium followed by its return toward normal, and a more gradual decrease in serum magnesium, are previously unreported. However, decreased levels of serum magnesium have been observed during acute myocardial infarction in humans (24). Reduced serum magnesium during myocardial infarction has been associated with increased ventricular arrhythmia (25). In autopsy specimens of myocardial tissue, the levels of magnesium and potassium are reduced and calcium is elevated after sudden cardiac death, as compared with those levels in tissues from hearts of patients dying from chronic heart failure or trauma (26,27). Magnesium has known electrophysiologic effects (28). Intravenous administration of magnesium has been used to treat cardiac arrhythmias. The decreases in calcium and magnesium may be important because magnesium is needed for the phosphorylation of adenosine triphosphate and calcium for excitation-contraction coupling in the myocardium. It is noteworthy that calcium channels are activated by epinephrine, thus increasing the entry of calcium into the cell (29). This might be the mechanism by which calcium decreases in this canine model.

The mechanisms for the shifts of potassium, calcium and magnesium and their electrophysiologic and electromechanical consequences are unknown, although all three actions play a role in the maintenance of the rest myocardial

membrane potential, the myocardial action potential and myocardial contractility.

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