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Arterial–Venous Magnesium Gradients in Hypovolemic Shock: An Indication of the Irreversible State (39100)

FRANK VALENCIC, BRUNO N. DODICH, ORVILLE A. HILL, JR., WILLIAM H. STRAIN, WALTER J. PORIES, AND ARTHUR FLYNN
(Introduced by J. W. Harris)

Department of Surgery, Cleveland Metropolitan General Hospital, Case Western Reserve University School of Medicine, Cleveland, Ohio 44109

Systemic magnesium (Mg) changes have been related to trauma and tissue injury. In human studies increased Mg levels varied directly with the severity of hemorrhagic shock (1). Similar elevated Mg values were reported in animal studies with a variety of physical insults (2, 3). These increases in serum Mg would reflect the liberation of cellular Mg with tissue destruction, which contents are vital for cell replication (4). The relationship of Mg to the degree of tissue injury, therefore, may indicate the usefulness of arterial–venous (A–V) Mg plasma gradients in defining the progression or reversal of cellular degradation.

Methods. Serial arterial and venous blood samples were made in stress dogs to test the A–V Mg plasma gradients as indicators of cell destruction and the lethal/reversible shock state. Both calcium (Ca) and Mg plasma levels were determined to allow for comparison between nonstress and stress related divalent cations. Twelve mongrel dogs divided into lethal oligemia and nonlethal oligemia groups of six animals each were monitored for arterial blood pressure, A–V Ca and Mg, electrocardiogram, hematocrit, and shed blood volume. All animals were anesthetized with intravenous sodium pentobarbital, 27 mg/kg, and were anticoagulated with heparin, 5 mg/kg. Artificial respiration was maintained throughout the monitoring period. Blood samples were taken from catheters placed in the descending aorta and inferior vena cava, whereas pressure monitoring and controlled bleeding were made with femoral arterial catheters. Three A–V blood samples were taken during the 60-min control period; the dogs were then bled into a reservoir to a mean blood pressure of 65 mm Hg at which time a fourth A–V sample was taken. Thereafter, A–V samples were taken at 30-min intervals during oligemia and/or recovery.

During the oligemic period, the lethally shocked dogs were constrained to a blood pressure of less than 80 mm Hg, whereas the reversibly shocked animals were held to a blood pressure of less than 90 mm Hg. No reservoir blood was returned to either group of animals, but the lethally shocked animals had further bleeding. The lethal shock dogs all expired within 3 hr of the onset of shock. The reversibly shocked animals were reinfused after 2 hr of oligemia, and the mean arterial blood pressure was increased to an average of 123 mm Hg during the hour postreinfusion. All animals in this group survived the 2-hour oligemia and were survivors when checked 2 days after the shock period. Ca and Mg levels were determined by atomic absorption spectroscopy with differential A–V levels being noted for the two elements. Pearson r correlations between arterial and venous plasma levels of calcium and magnesium were then tested for statistical significance.

Results. Tables I, II, III, and IV show the actual values, the normalized values, and the statistical dispersions in Mg and Ca plasma levels throughout all phases of both experiments. Figs. 1 and 2 show the sequential course of the group mean blood pressure, shed blood volume, and arterial and venous hematocrits for the lethally and reversibly shocked animals. Initial mean hematocrits in the lethal (44.4 ± 5.0) and reversible (39.2 ± 4.4) shock groups were not statistically different ($t = 2.0$; NS at 95% confidence limits). The final hematocrit differences, lethal (37.4 ± 1.26) and reversible (42.1 ± 5.68), demonstrate a greater eryth-

TABLE I. AVERAGE MAGNESIUM PLASMA LEVELS IN LETHAL SHOCK[a]

Time (Min)	−60	−30	0	5	30	60	90	120
Arterial (% Mg)	100[b]	96.4	97	107.6	115.8	116.5	124.3	124.9
SEM	0	2.7	2.3	5.31	5.63	2.46	6.15	9.55
Venous (% Mg)	100[c]	102.3	99.5	133	128	132	142.6	148.5
SEM	0	2.85	3.1	9.1	3.66	.98	4.9	7.89

[a] Tables I and II show the average Mg and Ca plasma values, of normalized 100% element levels, during lethal shock. Serial, normalized arterial–venous Mg and Ca plasma levels and their SEM are presented.

[b] 100% arterial level = 2.44 mg/100 ml.

[c] 100% venous level = 2.27 mg/100 ml.

TABLE II. AVERAGE CALCIUM PLASMA LEVELS IN LETHAL SHOCK

Time (Min)	−60	−30	0	5	30	60	90	120
Arterial (% Ca)	100[a]	105.3	104	100.2	96.4	99.6	96	100.2
SEM	0	2.8	1.9	1.3	2.7	4.2	5.06	4.45
Venous (% Ca)	100[b]	100.2	99.8	101	96	95.7	94.7	96.4
SEM	0	3.2	2.9	1.8	3.5	3.07	4.96	4.43

[a] 100% arterial level = 10.1 mg/100 ml.

[b] 100% venous level = 10.3 mg/100 ml.

TABLE III. AVERAGE MAGNESIUM PLASMA LEVELS IN REVERSIBLE SHOCK[a]

Time (Min)	−60	−30	0	5	30	60	90	120	150	180
Arterial (% Mg)	100[b]	91.3	95.1	102.3	109.4	107	111.9	113.4	101.7	99
SEM	0	3.8	2.2	3.3	6.73	3.87	5.7	5.42	5.97	7.1
Venous (% Mg)	100[c]	97.5	97.2	128.8	112.2	108	110.5	115.4	106.1	98.3
SEM	0	3.0	4.3	9.2	5.9	5.7	5.1	3.8	5.1	5.0

[a] Tables III and IV show the average Mg and Ca plasma values, of normalized 100% element levels, during reversible shock. Serial, normalized arterial–venous Mg and Ca plasma levels and their SEM are presented.

[b] 100% arterial level = 1.79 mg/100 ml.

[c] 100% venous level = 1.74 mg/100 ml.

rocyte dilution in the lethally shocked dogs ($t = 3.46$; S at 95% confidence limits) than in the reversibly shocked group.

The comparison of the A–V Ca and Mg differentials is illustrated in Figs. 3 and 4. Significant increases ($P < 0.05$) in the Mg values over control levels were noted in samples taken 5 min after the onset of hemorrhage in both groups. Lethally shocked animals demonstrated significant A–V Mg gradients throughout the entire oligemic phase ($P < 0.05$), whereas reversibly shocked dogs had a significant gradient only at the 5 min posthemorrhage sampling ($P < 0.05$). After that initial sample, all A–V Mg values were statistically comparable in the reversibly shocked dogs.

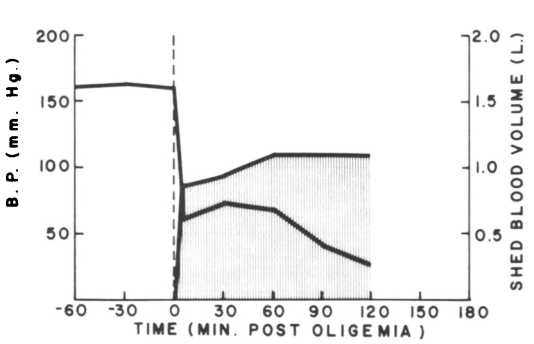
Insignificant changes in plasma Ca were monitored in both groups of animals during oligemia, as is also shown in Figs. 3 and 4. No A–V Ca plasma gradients were demonstrable during the entire experimental period.

Discussion. Increased plasma Mg levels can be attributed to two diverse, yet related processes. First, the addition of Mg into the vascular system by damaged cells containing Mg (4), and second, reduced renal Mg clearance (5). Constant A–V Mg gradi-

TABLE IV. AVERAGE CALCIUM PLASMA LEVELS IN REVERSIBLE SHOCK

Time (Min)	−60	−30	0	5	30	60	90	120	150	180
Arterial (% Ca)	100[a]	91.2	96.8	92.4	92.8	91.5	87	90.5	94	93.8
SEM	0	3.6	2.19	4.0	2.8	2.6	5.58	2.9	4.2	3.2
Venous (% Ca)	100[b]	98.7	101	100.2	95.4	93.1	92.7	93.5	97.3	95.7
SEM	0	2.9	3.8	3.38	2.3	2.4	2.93	2.4	4.6	4.0

[a] 100% arterial level = 13.79 mg/100 ml.
[b] 100% venous level = 13.19 mg/100 ml.



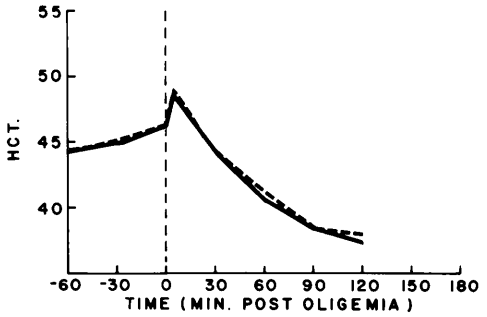
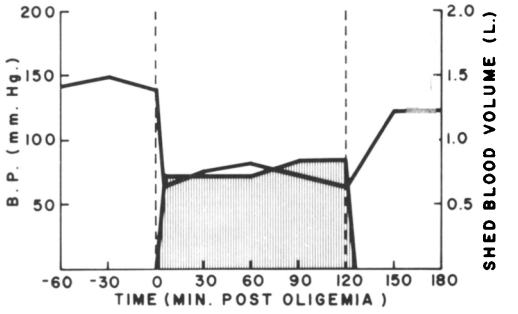


FIG. 1. Hemodynamic profile of lethally shocked dogs (n = 6), showing arterial blood pressure, shed blood volume, and both arterial (——) and venous (– –) hematocrits.



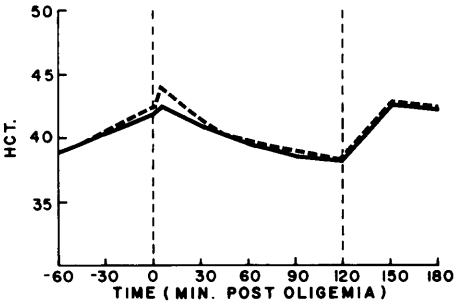


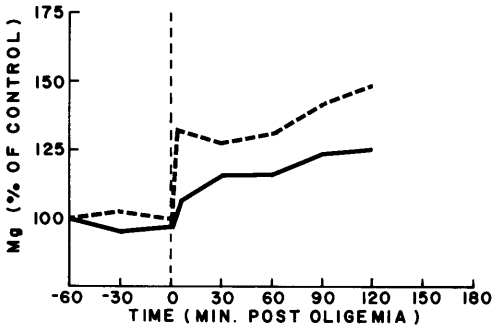
FIG. 2. Hemodynamic profile of reversibly shocked dogs (n = 6), showing arterial blood pressure, shed blood volume, and both arterial (——) and venous (– –) hematocrits.

ents and reduced renal Mg excretion in the lethally shocked animals accounts for the continual increase in Mg during the oligemic episode. Persistence of the plasma Mg gradient appears to reflect continuous destruction of cells.

In contrast, reversibly shocked animals show a nonpersistent plasma Mg gradient. This transient gradient and reduced renal Mg clearance results in an elevated, but relatively constant arterial plasma Mg level. Disappearance of the Mg gradient in the reversibly shocked animals 30 min after the onset of oligemia may be indicative of no further cell destruction.

Total absence of a plasma calcium gradient coupled with insignificant A–V plasma Ca concentration changes indicates an independent function for Ca in the development of hemorrhagic shock. This finding substantiates Barry's data (6) in similar studies on hemorrhagically shocked dogs.

Mg and Ca play important physiological roles in biological systems and exist in rela-



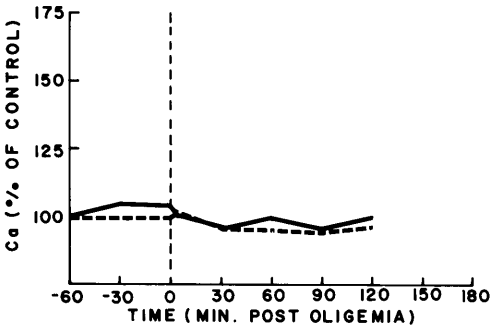
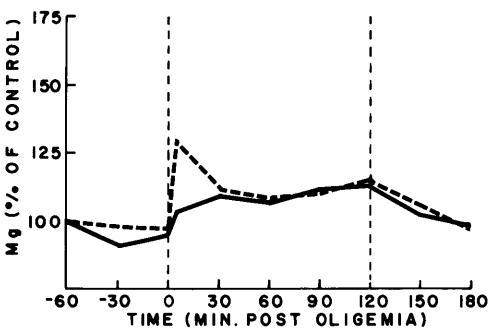


FIG. 3. Mean arterial (——) and venous (– –) magnesium (Mg) and calcium (Ca) in lethally shocked dogs.



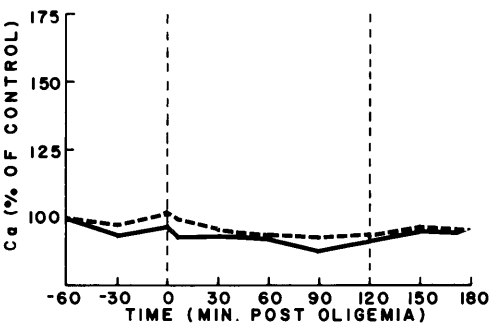


FIG. 4. Mean arterial (——) and venous (– –) magnesium (Mg) and calcium (Ca) in reversibly shocked dogs.

tively equal distribution, yet in hemorrhage, they appear to have very divergent action. The concept of an arterial–venous plasma magnesium gradient may be an important indicator of the severity of hemorrhagic shock, in fact, it may indicate the irreversible shock state.

Summary. Arterial–venous magnesium differences were examined in mongrel dogs stressed with reversible and lethal hypovolemia. Increases in serum Mg with hemorrhage have long been known to occur in both humans and animals, yet, increased blood Mg levels have not been viewed as an indicator of the irreversible shock state. The magnesium gradient was shown to be a good indicator of cell destruction which is consistent with lethal shock.

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