the present experiments were carried out not under conditions of spontaneous diuresis, but during infusion of a hypertonic solution of glucose, and this could weaken the diuretic response to the glucocorticoid.

LITERATURE CITED

1. V. M. Bryukhanov, Fiziol. Zh. SSSR, 63, 742 (1977).
2. Yu. I. Ivanov, Probl. Éndokrinol., No. 1, 92 (1965).
3. A. S. Oganesyan, Some Problems in the Hormonal Regulation of Renal Activity and Membrane Permeability [in Russian], Erevan (1968).
4. M. G. Eggleston, et al., J. Physiol. (London), 124, 623 (1954).
5. J. H. Miller, Proc. Soc. Exp. Biol. (New York), 84, 322 (1953).
6. J. A. Shannon et al., Am. J. Physiol., 133, 752 (1941).

EFFECT OF INTRAVENOUS INJECTIONS OF CALCIUM CHLORIDE ON EFFECTIVENESS OF INFUSION THERAPY OF ACUTE MASSIVE BLOOD LOSS

D. M. Sherman and I. T. Tsygura

UDC 616.151.11-085.31:546.41'131

Acute experiments on 70 dogs showed that in the late stage of response of the animal to acute massive blood loss neither blood transfusion nor infusions of calcium-free gelatinol or 0.9% NaCl could prevent death of the animals. Intravenous injections of 10% $CaCl_2$ solution immediately after the above infusion therapy led to survival of most of the animals.

KEY WORDS: infusion therapy; hemorrhagic shock in dogs; injection of $CaCl_2$.

In the late stages of the response of the body to acute blood loss, blood transfusions or infusion of colloidal and salt solutions do not always prove successful [8-10].

Considering that calcium ions play an important role in the regulation of cardiac activity [4, 7, 12, 14, 15], have the ability to increase the tone of the vagus nerves [1], and have a significant effect on heart muscle [3, 4], and the mechanism of transmission of nervous impulses and on enzyme systems [3], it seemed likely that intravenous injections of $CaCl_2$ solution would make the infusion therapy of acute massive blood loss more effective. To test this hypothesis the experiments described below were undertaken.

EXPERIMENTAL METHOD

Experiments were carried out on 70 unanesthetized dogs of both sexes and of different weights. Bleeding took place from the femoral artery for 3-5 min until the blood pressure had fallen to 40-45 mm Hg. The mean volume of the blood loss was 35 ml/kg body weight. In the course of the experiment the arterial and central venous pressures, heart rate, respiration rate, rectal and subcutaneous temperatures (electrothermometer), EEG (unipolar derivation with needle electrodes), ECG (standard lead II), and EMG (using needle electrodes from the posterior cervical muscles) were recorded. The indices were recorded on a four-channel 4ÉÉG-01 electroencephalograph; changes in spontaneous activity and the effect of photic stimulation (10 flashes/sec) and acoustic stimulation (1000 Hz) were analyzed. At the critical stages of the experiments the conjunctival vessels were photographed (with the MBS-2 microscope), and the erythrocyte count, hemoglobin concentration, hematocrit index, cardiac output (by the dye dilution method with T-1824) and the blood flow rate (by the lobeline method) were investigated. On the basis of these parameters the dynamics of the posthemorrhagic reaction could be assessed objectively. The main criteria of the efficacy of treatment were the survival rate and life span of the animals. A 10% solution of $CaCl_2$ was injected in a dose of 50 mg/kg at the rate of 2-3 ml/min after blood transfusion or infusions of plasma-substitute solution in the late stage of hemorrhagic shock.

Experimental Laboratory, L'vov Military Hospital. (Presented by Academician of the Academy of Medical Sciences of the USSR N. A. Fedorov.)

Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 86, No. 12, pp. 697-700, December, 1978. Original article submitted April 18, 1978.

0007-4888/78/8612-1624$07.50

TABLE 1. Effect of Intravenous Injections of $CaCl_2$ on Effectiveness of Infusion Therapy in Late Period of Hemorrhagic Shock (M ± m)

Series of experiments	Number of animals	Volume of blood loss, ml/kg	Outcome: survived	Outcome: period of survival until death of animals, h
I. Control	10	35,8±0,7	—	4,1±0,8
II. Reinfusion of blood	10	33,8±1,2	2	9,2±1,8*
III. Infusion of gelatinol	10	37,7±0,8	—	10,3±2,3*
IV. Infusion of 0.9% NaCl	10	35,9±1,6	1	13,2±2,3*
V. Reinfusion of blood and intravenous injections of $CaCl_2$	10	38,8±2,2	8*	27,5 и 16,0
VI. Infusion of gelatinol and intravenous injections of $CaCl_2$	10	38,2±0,8	8*	23,3 и 19,0
VII. Infusion of 0.9% NaCl and intravenous injections of $CaCl_2$	10	37,5±1,3	7*	10,6±4,2*

*$P < 0.05$ compared with control.

TABLE 2. Changes in Principal Physiological Indices Under Influence of Infusion Therapy and Intravenous Injections of $CaCl_2$ in Late Period of Hemorrhagic Shock (M ± m)

Series of experiments	Systolic arterial pressure, mm Hg	Central venous pressure, mm Hg	Heart rate, beats/min	Hematocrit index	Circulating blood volume, ml/kg	Erythrocyte count, millions	Lobeline time, sec	Respiration rate, breath/min	Temperature, °C: rectal	Temperature, °C: subcutaneous
I. Control:										
Initial values	137±5	−41±6	66±3	49±0,9	90±4	5,2±0,1	19±2	33±5	38,3±0,1	34,0±0,4
Phase of inhibition	41±3	−41±6	213±9	43±0,7	60±4	4,3±0,1	32±6	21±2	37,6±0,2	32,6±0,4
Period of stabilization	85±5	−40±5	231±9	41±0,9	59±3	4,0±0,1	29±3	22±2	37,7±0,2	32,4±0,4
II. Reinfusion of blood:										
Initial values	134±6	−34±7	71±7	47±0,1	87±6	4,8±0,1	18±4	25±3	38,4±0,1	35,9±0,4
Phase of inhibition	41±5	−24±6	182±7	44±0,9	58±7	4,3±0,1	34±7	20±2	36,8±0,2	33,1±0,2
Period of stabilization	68±7	−41±5	214±10	41±1,0	56±3	4,0±0,1	31±6	24±2	36,3±0,2	32,2±0,4
Before treatment	40±5	−18±4	198±10	40±1,0	51±3	4,0±0,2	34±5	23±5	35,9±0,2	32,7±0,2
30 min before end of experiment	49±14	−10±2	127±1	37±0,9	65±4	4,1±0,2	28±6	17±2	34,8±0,3	32,0±0,4
III. Infusion of gelatinol:										
Initial values	124±6	−38±4	72±2	51±2,0	92±4	4,9±0,2	20±2	34±4	38,2±0,1	33,0±0,5
Phase of inhibition	44±1	−40±4	201±13	45±2,8	59±3	4,2±0,3	29±3	24±3	37,0±0,1	32,1±0,4
Period of stabilization	78±7	−38±3	233±12	43±2,6	58±2	3,9±0,2	27±1	23±1	38,1±0,2	31,8±0,4
Before treatment	45±2	−42±3	239±12	44±2,6	51±2	4,2±0,3	38±3	21±3	37,8±0,1	31,4±0,4
30 min before end of experiment	75±10	−10±2	206±16	35±1,8	60±2	4,0±0,2	19±3	27±6	38,1±0,5	34,3±0,4
IV. Infusion of NaCl solution:										
Initial values	121±4	−38±5	71±3	50±1,1	92±4	5,1±0,1	17±1	34±4	38,3±0,2	33,7±0,5
Phase of inhibition	45±3	−41±5	213±11	45±1,8	62±5	4,6±0,2	23±2	20±3	37,9±0,2	32,4±0,4
Period of stabilization	83±4	−38±4	229±11	43±2,4	59±3	4,3±0,2	23±3	25±3	38,1±0,2	31,9±0,3
Before treatment	47±3	−41±3	220±8	45±1,6	52±2	4,6±0,2	32±2	25±3	37,9±0,1	31,5±0,4
30 min before end of experiment	80±9	−12±3	199±13	35±1,8	67±3	4,0±0,2	21±3	31±6	38,1±0,5	34,9±0,4
V. Reinfusion of blood + $CaCl_2$:										
Initial values	130±2	−20±3	68±6	50±9,3	92±2	5,4±0,5	18±4	38±8	38,2±0,2	34,6±0,8
Phase of inhibition	45±3	−43±8	214±4	45±5,4	60±4	4,8±0,6	34±6	29±5	37,4±0,3	33,9±0,9
Period of stabilization	69±5	−43±6	230±9	41±5,0	57±5	4,4±0,5	30±5	24±3	36,9±0,6	33,6±0,6
Before treatment	46±6	−46±5	224±10	44±5,8	52±4	4,5±0,7	34±6	24±2	36,6±0,6	33,4±0,5
30 min before end of experiment	113±5*	−10±3	91±11*	48±5,0*	86±8*	5,5±0,6*	24±5	18±2	36,2±0,7	33,0±1,4
VI. Infusion of gelatinol + $CaCl_2$:										
Initial values	127±3	−35±4	66±3	51±2,2	92±4	4,9±0,2	19±1	33±5	38,4±0,1	33,3±0,3
Phase of inhibition	43±1	−42±5	189±9	46±2,3	59±4	4,5±0,3	28±3	23±3	37,7±0,2	32,2±0,3
Period of stabilization	78±3	−39±4	225±7	44±2,3	58±3	4,3±0,2	35±4	27±2	38,0±0,1	31,6±0,3
Before treatment	41±1	−41±3	236±8	46±2,2	51±2	4,3±0,2	35±4	27±2	38,0±0,1	31,0±0,3
30 min before end of experiment	96±4	−11±4	168±4*	32±2,2	78±7*	3,5±0,2	18±2	27±3	38,4±0,3	35,1±0,4
VIII. Infusion of NaCl solution + $CaCl_2$:										
Initial values	140±3	−38±5	67±4	50±2,3	91±3	5,2±0,2	20±3	36±4	38,1±0,1	33,7±0,4
Phase of inhibition	45±2	−42±5	220±8	43±2,2	60±4	4,4±0,2	29±3	24±3	37,7±0,1	32,6±0,4
Period of stabilization	85±5	−39±4	232±10	41±2,2	58±2	4,2±0,2	25±3	26±3	38,2±0,1	32,4±0,4
Before treatment	49±2	−42±4	239±10	45±2,3	51±2	3,7±0,3	36±2	29±3	38,0±0,1	32,2±0,4
30 min before end of experiment	103±10*	−12±3	177±9	33±2,1	80±7*	3,7±0,3	18±2	25±4	38,3±0,4	35,1±0,5

Legend. Indices differing significantly from those in series of experiments in which animals were treated without intravenous injections of $CaCl_2$ ($P < 0.05$) marked by asterisk.

EXPERIMENTAL RESULTS

The results of series I (control) showed that acute massive blood loss caused a response in all the animals with a distinctly phasic course, as shown by changes in nearly all the parameters listed above. Blood loss was followed almost immediately by a phase of inhibition, after which an early period, a period of stabilization, and a late period could be easily differentiated. This last period was followed by a phase of collapse, followed by a terminal phase and death of the animals. The late period was characterized by a gradual and steady fall of the arterial and central venous pressures, an increase in tachycardia, an increase in the number of additional inspirations, an increase in the amplitude of the third-order waves, a further fall of temperature, disappearance of rhythm-binding responses and establishment of a regular rhythm of slow high-amplitude waves on the EEG, the appearance of bursts of high potentials against the background of very low EMG activity, the almost complete disappearance of S-T intervals on the ECG and displacement of this segment, and other manifestations of increasing impairment of the hemodynamics. A more detailed description of the dynamics of the posthemorrhagic response was described by the writers previously [11].

In series II the lost blood, after stabilization, was reinfused. A well-marked but brief improvement in the above parameters was observed. The positive effect of the treatment was reflected in a significant increase in the life span of the animals (Table 1).

In series III the lost blood was replaced by infusion of calcium-free gelatinol. The hemodynamic effect and the changes in the remaining indices did not differ significantly from those in the previous series. All the animals died at significantly later times than in the control series. In series IV the lost blood was replaced by infusion of 0.9% NaCl solution. On the whole, the changes in these indices and the outcome of the experiments did not differ from those with reinfusion of blood and infusion of the colloidal solution, as shown by the results in Table 2. In all these three series a significant improvement in the hemodynamic indices was not accompanied by restoration of the sinus arrhythmia or normalization of the ECG and EEG parameters, including recovery of the rhythm-binding responses to flashes or recovery of the circulation in the microcirculatory part of the vascular system. The conjunctival vessels remained dilated.

In the other three series, at the height of the hemodynamic effect of the reinfusion of the blood or infusion of gelatinol or salt solution, $CaCl_2$ solution was injected. After injection of the first portions of this solution a decrease in the heart rate, increase in the duration of S-T and T-P intervals, displacement of the ST segment toward the isoelectric line of the ECG, and the appearance of sinus arrhythmia were observed, indicating restoration of the functions of the higher levels of regulation of cardiac activity [2, 5]. After a short time the animals began to exhibit motor activity, and at that stage the experiment was ended. After removal from the table the dogs eagerly drank water and responded to external stimuli. However, this therapeutic effect in some of them was temporary and the typical course of late period of hemorrhagic shock soon recurred and the animals died.

Intravenous injections of $CaCl_2$ solution thus significantly improves the efficacy of transfusion and infusion therapy in the late period of hemorrhagic shock.

LITERATURE CITED

1. A. A. Abinder, N. K. Khitrov, et al., Fiziol. Zh. SSSR, No. 1, 117 (1975).
2. R. M. Baevskii, Physiological Methods in Astronautics [in Russian], Moscow (1965).
3. G. A. Langer, in: Metabolism of the Myocardium (Proceedings of a Symposium) [in Russian], Moscow (1975), pp. 195-209.
4. F. Z. Meerson and V. I. Kapel'ko, Kardiologiya, No. 7, 43 (1974).
5. V. A. Negovskii, Fundamentals of Resuscitation [in Russian], Moscow (1966).
6. V. V. Parin, R. M. Baevskii, et al., Space Cardiology [in Russian], Moscow (1967).
7. V. V. Parin and F. Z. Meerson, Kardiologiya, No. 4, 5 (1971).
8. I. R. Petrov and G. Sh. Vasadze, Irreversible Changes in Shock and Blood Loss [in Russian], Leningrad (1972).
9. G. M. Solov'ev and G. G. Radzivil, Blood Loss and Regulation of the Circulation in Surgery [in Russian], Moscow (1973).
10. I. Teodorescu-Eczarcu, General Surgical Agressology [in Russian], Bucharest (1972).
11. D. M. Sherman, The Problem of Traumatic Shock [in Russian], Moscow (1972).
12. L. E. Bailey and P. E. Dresel, J. Gen. Physiol., 52, 969 (1968).

13. H. D. Colp, Proc. Natl. Acad. Sci. USA, 43, 137 (1969).
14. K. I. Shine, S. D. Serena, and G. A. Langer, Am. J. Physiol., 221, 1408 (1971).
15. S. Winergrad, J. Gen. Physiol., 51, 65 (1968).