VASCULAR DYNAMICS IN CONTROLLED HYPOTENSION:

A STUDY OF CEREBRAL AND RENAL HEMODYNAMICS AND BLOOD VOLUME CHANGES*

GEORGE C. MORRIS, JR., M.D., JOHN H. MOYER, M.D.,
HARVEY B. SNYDER, M.D., AND B. W. HAYNES, JR., M.D.

HOUSTON, TEXAS

FROM THE DEPARTMENTS OF SURGERY, PHARMACOLOGY AND MEDICINE, BAYLOR UNIVERSITY COLLEGE OF MEDICINE, HOUSTON, TEXAS

THE USE OF CONTROLLED hypotension in surgery has gained rapid momentum during the past five years in Britain and on the European Continent.[2-7, 9, 12, 15, 16] This followed the report of Griffith and Gillies,[6] who reduced the blood pressure by blockade of the sympathetic nervous system with high spinal anesthesia. The use of ganglionic blocking agents[3] to obtain a similar degree of hypotension has further increased the applicability of the method because of its simplicity. In spite of the marked reduction in blood pressure which has been employed in numerous surgical clinics using this technic there is a paucity of reported studies regarding the altered vascular dynamics, particularly in such critical vascular beds as the brain and kidney.[10, 11] Previous work has shown that there is no significant change in cerebral blood flow in normotensive individuals with small reductions in blood pressure[8] following a single injection of dihydroergocornine. However, there have been no reports of observations on the cerebral circulation at the marked hypotensive levels which are employed in hypotensive surgery. The current investigation is concerned primarily with measurements of cerebral blood flow and cerebral oxygen consumption in a group of surgical patients with marked hypotension induced by hexamethonium. This study was initiated in order to determine, if possible, the safe blood pressure ranges which may be employed in controlled hypotensive surgery. Additional studies include differential renal function and blood volume measurements.

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METHODS

Cerebral Hemodynamic Studies. Hexamethonium chloride† was administered as a continuous intravenous infusion (500 mg. of hexamethonium per 1000 cc. 5 per cent glucose in water) to the unanesthetized, horizontally supine patient. The patients were not anesthetized in order that disturbances in cerebral function could be immediately recognized, thus increasing the safety factor in these initial studies. Continuous mean blood pressure recordings were made from a mercury manometer connected to a needle inserted in the femoral artery.

Cerebral blood flow studies employing the nitrous oxide technic[13] were done on five normotensive and three mildly hypertensive surgical patients (Table IA). Ob-

† Supplied as Hexameton (parenteral) by Burroughs Wellcome and Company, and as Methium (parenteral) by Chilcott Laboratories, Inc.

servations were made during a control period and again one hour following the induction of hypotension in the supine position. Observations were again made immediately after the induction of hypotension (period H1, Table II) after one hour (period H2), after two hours (period H3),

TABLE IA. *Effects of Blood Pressure Reduction on Cerebral Hemodynamics and Cerebral Oxygen Uptake.*

Subject	Mean Blood Pressure mm. Hg.†		Cerebral Blood Flow cc./100 gm./brain/min.		Cerebral Vascular Resistance*		Cerebral O_2 Uptake cc./100 gm./brain/min.	
	C	H	C	H	C	H	C	H
D. D.	125	60	51	43	2.5	1.4	4.0	3.6
J. G.	111	66	51	30	2.2	2.2	2.9	2.0
B. F.	100	65	49	36	2.0	1.8	2.5	2.2
D. L.	124	63	75	36	1.7	1.8	4.1	3.6
B. C.	101	78	64	45	1.6	1.7	2.8	2.0
J. Z.	76	56	52	47	1.5	1.2	2.5	2.7
H. M.	96	54	56	40	1.7	1.4	2.8	3.1
G. T.	100	56	54	33	1.9	1.7	3.6	2.8
Mean	104	62	57	39	1.9	1.7	3.2	2.8
Mean for % of Control		61		70		89		88

*—Cerebral vascular resistance equals mean arterial blood pressure divided by cerebral blood flow.
†—Mean blood pressure—direct arterial manometry.
H—After blood pressure reduction for one hour.
% of Control—Mean value for per cent change in each patient. Control value equals 100 per cent.

TABLE IB. *The Effect of Hypotension on Arterial O_2 and CO_2 and Cerebral Venous (Jugular Bulb) O_2 and CO_2.*

Subject	Arterial O_2 Vol. %		Venous O_2 Vol. %		Cerebral A-V O_2 Difference Vol. %		Arterial CO_2 Vol. %		Venous CO_2 Vol. %		Arterial Partial Pressure CO_2 mm. Hg.	
	C	H	C	H	C	H	C	H	C	H	C	H
D. D.	14.6	12.5	6.7	4.1	7.9	8.4	35.6	37.6	43.6	44.6	38	46
J. G.	17.4	16.2	11.7	9.7	5.7	6.5	37.2	40.0	43.4	45.1	41	44
B. F.	12.9	11.7	7.7	5.5	5.2	6.2	44.3	46.0	51.0	53.0	54	43
D. L.	17.0	16.5	11.6	6.4	5.4	10.1	42.0	41.5	48.0	47.7	45	38
B. C.	12.2	11.7	7.8	7.2	4.4	4.5	45.6	46.6	48.6	51.2	31	34
J. Z.	13.4	12.9	8.6	7.2	4.8	5.7	44.3	43.0	46.6	48.6	34	35
H. M.	14.1	13.9	9.1	6.1	5.0	7.8	45.1	43.4	49.3	51.5	36	38
G. T.	17.7	16.3	11.0	7.9	6.7	8.4	44.5	43.0	52.5	53.4	40	43
Mean	14.9	14.0	9.3	6.8	5.6	7.2	42.3	42.6	47.9	49.4	41	40
Mean for % of Control		94		73		129		101		103		99

See Table IA for key to abbreviations.

Renal Hemodynamic Studies. Renal function studies were carried out on 12 surgical patients using inulin clearance as a measure of glomerular filtration rate (GFR) and low concentration (2 to 4 mg. per cent) of para-aminohippurate (PAH) to measure renal plasma flow employing methods and technics previously described.[11] Control determinations are averages of three ten-minute collection periods. and after three hours (period H4). Each of these observations (H1 to H4) are averages of two to four ten-minute collection periods. All observations were made with the patient in the supine position. Simultaneous cerebral blood flow studies were made on four of these patients (Tables IA and IB) and blood volume determinations were made on all but two patients (Table III).

Observations on Blood Volume. Blood volume estimations were made in 16 surgical patients before induction of hypotension and again after induction. The time interval (after inducing hypotension) for the second blood volume determination was one hour for 11 patients and two to four hours for the remaining five. A modification of the method of Allen and Kelley[1] was used in which 5 cc. of radioactive iodinated human serum albumin (10 microcuries per cc.) were injected intravenously. Fifteen to 20 minutes later 10 cc. of arterial blood was collected for determinations of radioactive iodine content. Blank arterial blood samples were obtained prior to the injection of radioactive iodine in subsequent blood volume determinations. Radioactive counting was done in a Texas well counting chamber. All lots of radioactive iodinated human serum albumin were checked for adequacy of tagging by 24 hour urine excretion studies. Observations on renal hemodynamics were made simultaneously in nine patients, and studies on cerebral blood flow were done on eight patients. All three studies (cerebral, renal and blood volume) were done simultaneously on four of the patients (J. G., D. L., J. Z., and G. T.).

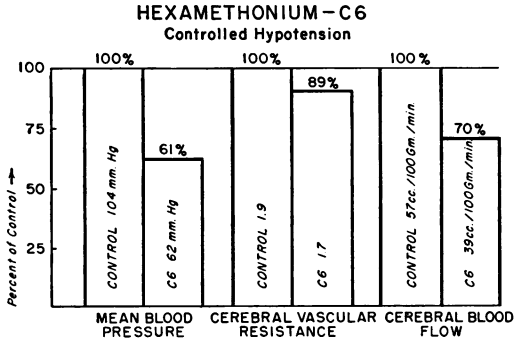

FIG. 1. The effect of blood pressure reduction on cerebral hemodynamics – average values expressed graphically in terms of percent of control observations.

RESULTS

The effects of hypotension on cerebral hemodynamics are summarized in Tables IA and IB. The reduction in mean blood pressure in the various subjects ranged from 23 to 52 per cent and averaged 39 per cent of the control observations. This was associated with an average reduction in cerebral vascular resistance of 11 per cent and the cerebral blood flow decreased 30 per cent. Despite a rather consistent reduction in cerebral blood flow, cerebral oxygen consumption was reduced only 12 per cent because of a 29 per cent increase in arterio-venous oxygen difference indicating increased extraction of oxygen per unit volume of blood. The arterial pH was not altered significantly and the partial pressure of arterial carbon dioxide (pCO_2) showed variations, but these were very erratic and not always in the same direction.

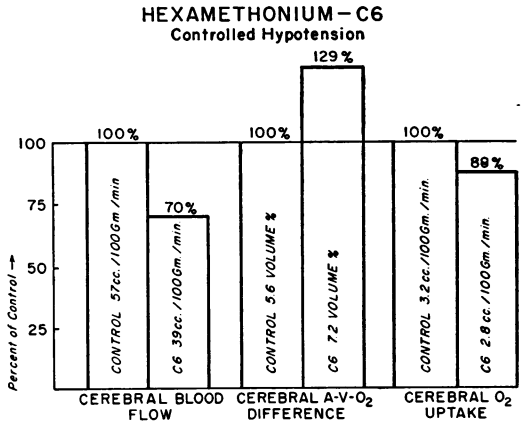

FIG. 2. The effect of blood pressure reduction on cerebral oxygen metabolism – average values expressed graphically in terms of percent of control observations.

The data from the renal studies are summarized in Table II. In the immediate hypotensive period (first 30 minutes after induction of hypotension) the mean blood pressure was reduced to an average of 67 per cent of control ranging from 54 per

cent to 80 per cent in the various subjects. After one hour (period H2) the average mean blood pressure continued in the same general hypotensive range (65 per cent of control ranging between 53 per cent and 82 per cent). An equivalent degree of hypotension was maintained in the patients who were observed for two and three hours respectively. The glomerular filtration rate (mean of percent of control values) fell to 74 per cent in the immediate hypotensive period. This increased slightly to 83 per cent after two hours of blood pressure reduction, and again fell to 78 per cent after three hours. Renal plasma flow likewise showed an initial drop to 74 per cent of the control value, but by contrast to GFR, this was followed by a steady rise, to 89 per cent after one hour period, 105 per cent by the second hour, and 124 per cent after the three-hour period. Hence, the filtration fraction decreased progressively after the initial rise. Urine volume was markedly reduced during the entire period of observation. In the immediate hypotensive period the mean value for the group was 20 per cent of the control, at one hour 21 per cent, at two hours 16 per cent, and at three hours 15 per cent.

On the average, the hypotensive blood volume as determined with radioactive iodine was increased 12 per cent over the control. The red cell mass increased 5 per cent and the plasma volume increased 17 per cent. In these studies, the average blood loss (as measured samples) in the period between the control and the hypotensive blood volume determinations was 326 cc. Adding this loss to the determined increase in blood volume resulted in an estimated average percent increase in blood volume of 17 per cent during hypotension.

TABLE II. *Effects of Blood Pressure Reduction on Glomerular Filtration Rate and Renal Plasma Flow.*

Subject	Mean Blood Pressure					Glomerular Filtration Rate					Renal Plasma Flow					Filtration Fraction				
	C	H1	H2	H3	H4	C	H1	H2	H3	H4	C	H1	H2	H3	H4	C	H1	H2	H3	H4
J. G.	117	73	67			105	54	67			473	314	367			.22	.17	.18		
D. L.	126	68	68			107	29	63			981	136	475			.11	.21	.13		
M. G.	104	80	82			92	77	88			372	363	354			.25	.21	.25		
J. M.	105	68	60			111	80	75			895	385	596			.12	.21	.13		
J. Z.	78	55	64	63		112	58	85	100		688	175	410	548		.16	.33	.21	.18	
G. T.	100	62	59	69		134	119	128	116		709	498	879	744		.19	.24	.15	.16	
J. C.	118	83	79	74	81	142	76	129	144	122	588	238	610	758	709	.24	.32	.21	.19	.17
L. F.	88	70	71	63	66	165	168	138	89	67	644	847	781	447	945	.26	.20	.18	.20	.07
B. G.	85	62	58	60	58	109	78	76	85	100	538	535	465	596	817	.20	.15	.16	.14	.12
M. P.	86	52	53	55	58	87	127	65	85	90	747	1052	780	711	641	.12	.12	.08	.12	.14
R. B.	131	86	69	64	63	67	43	39	49	44	390	318	365	573	445	.17	.14	.11	.09	.10
Mean	103	69	66	64	65	112	83	87	95	85	639	442	553	625	711	.19	.21	.16	.15	.12
Mean for % of Control		67	65	67	65		74	76	83	78		74	89	105	124		121	90	82	67

C—Control.
H1—Immediate hypotensive period.
H2—One hour of hypotension.
H3—Two hours of hypotension.
H4—Three hours of hypotension.

DISCUSSION

These studies indicate some of the compensatory mechanisms which operate during controlled hypotension. Hafkenschiel[8] showed that with only a 17 per cent reduction in mean blood pressure, compensatory cerebral vasodilatation permitted a normal cerebral blood flow. Furthermore, he found no reduction in jugular oxygen content. In our group of eight patients with an average reduction in mean blood pressure of 39 per cent, cerebral blood flow decreased 30 per cent in spite of an 11 per cent reduction in cerebral vascular resistance. Moreover, the second compensatory

mechanism, increased arterial-venous oxygen difference of 29 per cent, failed to compensate completely for the hypotensive state. A resultant decrease in cerebral oxygen consumption of 12 per cent took place. These changes are represented graphically in Figures 1 and 2.

tion following hexamethonium which has been previously described,[11] persisted throughout the three hour hypotensive studies. This is certainly a consideration to be borne in mind should a hemolytic transfusion reaction occur during controlled hypotension.[14]

TABLE III. *Effect of Blood Pressure Reduction on Blood Volume.*

Subject	Age	Sex	Blood Loss During Study CC.	Study*	Blood Volume C	Blood Volume H	Red Cell Mass C	Red Cell Mass H	Plasma Volume C	Plasma Volume H
D. D.	54	F	393	O	4377	4043∓	1742	1455	2635	2585
J. G.	49	M	482	Ox	5124	4844∓	2285	2017	2839	2827
B. F.	43	M	326	O	5005	5402∓	1506	1680	3499	3722
D. L.	24	M	465	Ox	5815	6668∓	2632	2820	3183	3848
J. Z.	30	M	405	Ox	5578	8050∓	2270	2950	3308	5100
H. M.	52	M	462	O	5769	8610∓	2595	3556	3174	5054
G. T.	30	M	620	Ox	5979	6585∓	2700	2857	3279	3727
E. D.	28	M	200	—	5380	6680∓	1855	2210	3525	4470
B. C.	19	M	512	O	7300	8190∓	2542	2612	4758	5578
D. J.	24	F	420	..	4425	4775∓	1747	1685	2678	3090
J. M.	26	M	110	x	6480	6820∓	2852	3010	3628	3810
L. F.	28	M	120	x	7140	7635∓∓	3185	3280	3955	4355
M. G.	18	M	140	x	4280	4494∓∓	1868	1773	2412	2721
J. D.	41	M	145	..	5710	6049∓∓	2525	2570	3185	3470
R. B.	25	F	215	x	3393	3495∓∓	1358	1337	2035	2158
M. P.	48	M	195	x	4750	4984∓∓	2010	1943	2740	3041
Mean Value			326		5407	6083	2230	2360	3177	3722
Mean for % of Control						112		105		117

See Table 2 for key to abbreviations.

*—0—represents cerebral flow done concurrently.

x—represents renal function done concurrently.

∓—performed one hour after induction of hypotension.

∓∓—performed 2-4 hours after induction of hypotension.

$$\% \text{ Increase} = \frac{\text{Value after blood pressure reduction}}{\text{Control Value}} \times 100; \text{ Control} = 100\%.$$

In the immediate hypotensive state there appears to be a relative differential vasoconstriction in the kidneys indicated by the abrupt drop in the renal plasma flow to 74 per cent of control. This increase in the renal vascular resistance gradually diminishes until after three hours of hypotension, the renal plasma flow actually increased in four out of five patients (average 124 per cent of control). At the same time the glomerular filtration rate, which was reduced to 74 per cent in the acute readjustment period, failed to return to normal with continued hypotension. The acute antidiuretic effect of blood pressure reduc-

The increase in blood volume would appear to represent still another compensatory reaction to controlled hypotension by ganglionic blockade. This hypervolemic response may be the result of a lowered capillary diffusion pressure due to decreased blood pressure, utilization of the plasma envelope surrounding the axial stream of corpuscles, or due to opening up of vascular reservoirs. One or both of the first two possibilities seem more likely in view of the fact that the increase in blood volume was predominantly a reflection of increased plasma volume. Only two of the 16 subjects failed to show a gain in blood

volume. It may be coincidental that both were moderately hypertensive. From Table III it is readily apparent that a small and gradual blood loss up to 600 cc. during controlled hypotension is adequately replaced.

SUMMARY AND CONCLUSIONS

1. The effects of hexamethonium induced hypotension on cerebral blood flow and cerebral oxygen consumption, renal function and blood volume were determined in a series of surgical patients.

2. A significant decrease in cerebral blood flow followed marked depression in the mean blood pressure in spite of a decrease in cerebral vascular resistance. Cerebral oxygen consumption was only slightly decreased due to a more complete extraction of oxygen from the blood flowing through the brain.

3. Initially, glomerular filtration rate and renal plasma flow were both depressed. However, after two to three hours of maintained hypotension, renal plasma flow returned to control levels whereas glomerular filtration rate remained depressed. Hexamethonium induced hypotension decreased urine formation.

4. Blood volume was slightly increased due predominately to an increase in plasma volume.

5. There appears to be little danger of cerebral or renal anoxia in the supine patient with a mean blood pressure as low as 55 mm. Hg. when employing hexamethonium induced controlled hypotension.

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