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THE EFFECT OF THE UPRIGHT POSTURE UPON HEPATIC BLOOD FLOW IN NORMOTENSIVE AND HYPERTENSIVE SUBJECTS ¹

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INTRODUCTION

The upright posture imposes a strain upon the cardiovascular system, chiefly as a result of its hydrostatic effects in the lower half of the body which, if unopposed, tend to produce hypotension in the upper half. These hydrostatic effects normally are counteracted by autonomic vasomotor adjustments, particularly in the splanchnic region. For example, the upright posture in man usually causes a reduction of renal blood flow (2). However, as yet no direct evidence has been reported concerning its effects upon the largest remaining portion of the splanchnic circulation, namely that draining through the liver. The present communication reports measurements of "hepatic blood flow" obtained with the bromsulfalein (BSP) extraction method (3) in normotensive and hypertensive subjects studied in the supine, in the upright, and again in the supine position.

METHODS

The estimated hepatic blood flow (EHBF) was measured by the intravenous catheterization method of Bradley and associates (3). The continuous infusion of BSP, was most easily maintained at a constant rate in both the horizontal and upright positions by suspending the infusion flask from a pole attached to the tilt table at such an angle that the flask remained at the same distance above the level of the subclavian vein when the table was horizontal or tilted up at 75°.

The subjects were hospital patients selected for study either because they had essentially normal cardiovascular systems or had arterial hypertension without evidence of cardiac, renal or hepatic insufficiency. All were studied in the basal state, at first supine, then tilted (passively) into the upright (75°) position for periods of 10 to 25 minutes (unless weakness and hypotension supervened), and finally, supine again. They were requested to remain as relaxed and motionless as possible throughout the test. Arterial pressure and pulse rate were measured either by the usual clinical methods or (in Cam, Aye and Dun) with a Hamilton manometer (4) at short intervals during each experiment.

Spot roentgenograms of the hepatic area were taken in each patient before, during, and after the upright tilt to demonstrate that the catheter remained properly placed in the same position near the center of the right lobe of the liver. To avoid possible errors due to mechanical and hydrostatic disturbances incident to changing the position of the subject, no result was computed on blood samples obtained within three minutes after a tilt, except for a few determinations made on blood samples that were taken immediately after a quick return to the horizontal position necessitated by faintness of the patient. As noted in Table I, such determinations have been related to the period just before rather than after this change of position because there appeared to be a time lag of one to two minutes before there was evidence of any acute change in hepatic blood flow as reflected in altered concentrations of BSP in the blood samples. After this time lag, however, considerable changes in serum BSP concentration could take place with great rapidity, especially when the subject had been tilted from the supine to the upright position. About four minutes after a tilt the trend of the BSP levels became more steady and the results after this time were accepted as more reliable measurements of an equilibrium state than those obtained earlier after a change in position. Furthermore, some subjects tolerated the upright position easily (top of Table IA and IB) and the results in them during upright tilting were regarded as more reliable than in the less stable subjects, some of whom fainted (bottom of Table IA and IB, and Figure 3).4

An effort was always made to draw the last pair of blood samples in each period as late as possible before a change in tilt table position. All estimates of rate of blood flow were calculated for the actual times of sampling and on the observed rather than the interpolated

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⁴ Only those data obtained after four minutes in a given position, and without fainting, are included in the statistical analysis in Table II.

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Effects of the upright posture upon estimated hepatic blood flow (EHBF), mean (half systolic plus diastolic) arterial pressure, calculated hepatic-portal resistance (HPR) and pulse rate in normotensive (A) and hypertensive (B) subjects, arranged in order of their relative adaptability

		Pulse rate (Beats/min.)		72 74	18	102 96 96	888	92 84 84	102 82 84	88	88					
tural response) to the upright posture	overy period	HPR (mm. Hg/ cc./sec./ 1.73 sq. m.)		3.2 3.6	4.6 	4.1 3.0 3.4	6.0 5.8 5.8	6.2 3.8 5.8	2 6.7 6.6	6.1	8.3 6.3					
	position, Rec	Mean arterial pressure (mm. Hg)		100 103	92 1	95 95 101	112 112 105	97 98 99	102 98 100		80 80					
	Horizontal	EHBF (cc./min./ 1.73 sq. m.)		1,858 1,713	1,210 1,155 	1,381 1,900 1,807	1,115 1,247 1,094	9 44 1,535 1,034	142* 874 912	962 	644 864					
		Minutes after tilt-back		8 4 15 4	9 <u>5</u> 0	5 114 18	3 7 14 4	3] 19] 31	3 <u>4</u> 84 15	5	7 3 13 4					
		Pulse rate (Beats/min.)		10 4 98	888	120 132 138	132	108 104	114	~	114					
	Upright (75°) position	HPR (mm. Hg/ cc./sec./ 1.73 sq. m.)		5.1 4.1	4.8 4.5 1.5	4.5 3.9 5.0 4.5	7.8	م 5.5 5.5	6.5	~	4.9 ?					
f poor post		Mean arterial pressure (mm. Hg)	(A)	97 90	106 100 100	866101 101 102	881	78 91 89	88	<u>-</u>	96 2					
and signs o		EHBF (cc./min./ 1.73 sq. m.)		1,143 1,312	1,339 1,375 1,466	1,319 1,505 1,203 1,381	762 680	50* 796 978	818† 	703*‡	1,174*‡ 505					
smotoms		Minutes after tilt-up	•	4 4 11	5 13 21	47 1 13 18	134	6 21 21	\ N	- 1 0	τς ας					
(freedom from s	riod	Pulse rate (Beats/min.)							68 76	85	9 <u>6</u>	888	888	88	88 88	72 72
	n, Control p	HPR (mm. H <u>e</u> / cc./sec./ 1.73 sq. m.)												3.1 3.6	2.3	3.4
	zontal positio	Mean arterial pressure (mm. Hg)		98 103	8	101	106 05	820	103	98 95	81 84					
	Hori	EHBF (cc./min./ 1.73 sq. m.)		1,92 4 1,716	2,600	1,762 1,603 —	1,500 1,411 —	1,107 2,164	1,101 1,082 	920 724	1,126 1,0 4 0					
	Patient	Age Sex Surface area (sq. m.)		Ema 39 M 1.70	0ls 32 M 1.89	Sil M 1.98	Tef M 2.08	Gio M 1.78	Car 24 M 1.76	Fau 28 M 2.07	McC 22 M 1.76					

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	Pulse rate (Beats/min.)	-	68 64 65	64	8	72 75 75	8000		26 56			
position, Recovery period	HPR (mm. Hg/ cc./sec./ 1.73 sq. m.)		8.4 7.1 6.2	8.5	6.0 	12.0 8.3 8.4	3.1 2.7 3.9	1	7.4 7.0			
	Mean arterial pressure (mm. Hg)		193 188 190	134 130 	156 -	152 170 160	136 143 133	·	168 168			
Horizontal	EHBF (cc./min./ 1.73 sq. m.)		1,380 1,591 1,844	949 892 -	1,036 900 —	768 1,224 1,141	2,650 3,164 2,050	1,575 1,347	1,363 1,444			
	Minutes after tilt-back		3 4 13 4 23 4	12	5 	3 10] 17	4 } 14 24	7 18	10] 22]			
	Pulse rate (Beats/min.)		86 84 86	84 87 88	88 88 83	90 112 108	72 84 ?	115 120	69 69			
aition	HPR (mm. Hg/ cc./sec./ 1.73 sq. m.)	(B)	7.4 8.9 7.6	12.0 8.4 11.0	9.8 9.7 10.0	18.0 12.0 10.0	8.7 11.0 11.0	13.0 16.0	8.5 10.0			
ight (75°) po	Mean arterial pressure (mm. Hg)		(B)	(B)	(B)	179 180 185	141 137 141	175 171 170	174 165 163	127 128 131	184 161	164 179
Upt	EHBF (cc./min./ 1.73 sq. m.)				1,450 1,211 1,461	702 979 760	1,072 1,059 998	566 825 969	876 713 694	859 586	1,154 1,041	
	Minutes after tilt-up		3 8 18	6 16 24 }	6 11 16	3 143 143	7 12 20 }	\$0 ¢0	6 10			
eriod	Pulse rate (Beats/min.)		68	64 	20 	76	60	68 68	58 64			
zontal position, Control p	HPR (mm. Hg/ cc./sec./ 1.73 sq. m.)					6.8 1.2	8.2 6.6	9.0	8.0 6.3	5.4 4.9 	9.7 8.0	6.5 8.6
	Mean arterial pressure (mm. Hg)			183 180 	131 142 —	167 	162 152 	133	174 176	159 177		
Hori	EHBF (cc./min./ 1.73 sq. m.)		1,624 1,503 	961 1,298 	1,118 	1,217 1,440 	1,466 1,590 	1,077 1,312	1,462 1,227			
Patient	Age Sex Surface area (sq. m.)		McC 43 M 1.75	She 51 M 2.02	Cam 51 M 1.71	Val 37 M 2.05	Max 43 M 2.21	Ric 33 M 1.91	Dea 54 M 1.82			

TABLE I—Continued

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Patient	Hori	zontal positic	m, Control p	eriod		Upri	ight (75°) po	sition			Horizontal	position, Rec	overy period	
Age Sex Surface area (sq. m.)	EHBF (cc./min./ 1.73 sq. m.)	Mean arterial pressure (mm. Hg)	HPR (mm. Hg/ cc./sec./ 1.73 sq. m.)	Pulse rate (Beats/min.)	Minutes after tilt-up	EHBF (cc./min./ 1.73 sq. m.)	Mean arterial pressure (mm. Hg)	HPR (mm. Hg/ cc./sec./ 1.73 sq. m.)	Pulse rate (Beats/min.)	Minutes after tilt-back	EHBF (cc./min./ 1.73 sq. m.)	Mean arterial pressure (mm. Hg)	HPR (<i>mm. Hg</i> / <i>cc./sec./</i> 1.73 sq. m.)	Pulse rate (Beats/min.)
						(B)	Continu	ed						
Gol 31 M 1.81	1,095 980	179 177	9.8 11.0	84 78	ا و	840	158 —	11.0	6	4 9 19 4 19	802 1,123 1,215 1,168	174 175 176 176	13.0 9.4 8.7 9.0	72 75 75
Pau 36 M 1.84	1,964	124	3.8	8	1 2	1,125	123	9.9	8	8233.3	1,895 1,505 1,750	119 114 126	3.8 4.5 3.8	60 64 75
Aye 51 M 1.86	1,409 1,408	164	7.0	12	- 2	863†	100	2.0	62	6 21 1	772 928 916	120 125 131	9.3 8.1 8.6	58 55 53
Dun 30 M 1.82	1,067	115	6.5	84	ñ	658†	~	4	~	4 12 4	750 953	124 104	9.9 6.5	81 90
Col 28 M 1.72	1,039 864	174 173	10.0 12.0	88	[4]	740‡	102	8.9	19	374 4 374 37	752 808 1,478 1,164	139 170 172 169	11.0 13.0 7.0 8.7	22 88 90 90 88 90 90 90 90 90 90 90 90 90 90 90 90 90
* This ' is deleted fr	value was (om the stand	obtained du tistical ana moles for F	lring a rapi Jysis (Tabl JHBF take	id rise (more e II). n. and imme	than 0.0 ediatelv t	006 mg./cc. bilted back)	/min.) in t horizontal.	the periphe	ral venous s	erum con	centration (of BSP. I	t is questic	nable, and

TABLE I-Continued

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Patient faint, tilted back horizontal, and samples for EHBF taken immediately. Patient had severe headache and excitement. values for serum concentration of BSP. Rate of change (ΔP) in the peripheral venous or (in Cam, Aye and Dun) arterial concentration of BSP was taken as the calculated average for the preceding period in each instance. This value never exceeded 0.0006 mg./cc./min., except in four instances when the subject had been hypotensive ⁵ (Table I). Blood volumes were calculated by the method of Gibson and Evans (5). All estimates of hepatic blood flow were corrected for standard surface area (1.73 sq.m.). Hepatic portal resistance (HPR) was calculated simply by dividing the "mean" (one-half systolic plus diastolic) arterial pressure by the EHBF per second.

A cold pressor test (6)—immersion of one hand in ice water for one minute—was applied to six (four normotensive and two hypertensive) subjects in the horizontal position after a period of recovery from the effects of the upright position. This was abandoned later because it was found to produce only equivocal effects upon EHBF.

RESULTS

A detailed presentation of data is given in Table I and a statistical summary in Table II. In both normotensive subjects (Table IA, Figure 1) and hypertensive patients (Table IB, Figure 2) the EHBF decreased following the tilt from the horizontal to the upright position. The decreases in

⁵ These data were omitted from the statistical analysis in Table II.



FIG. 1. CHART OF EHBF, ARTERIAL PRESSURE AND Pulse Rate in a Normotensive Subject (Sil), in the Horizontal, Upright, and Again in the Horizontal Position

"Mean" arterial pressure (half systolic plus diastolic) is indicated by the open circles and interrupted line. At the first vertical line, the subject was tilted upright (75°) and at the second, horizontal again.



FIG. 2. CHART OF EHBF, ARTERIAL PRESSURE AND PULSE RATE IN A HYPERTENSIVE PATIENT (VAL) Other notations as in Fig. 1.

EHBF were usually not associated with proportionate changes in mean arterial pressure, so that calculated hepatic-portal resistance (HPR) increased. Comparing only equilibrium values (Table II) the EHBF (cc./min.) decreased on the average from 1,713 to 1,070 in the normotensive group, from 1,357 to 960 in the hypertensive group, and from 1,499 to 1,004 in the combined groups. During the upright period, the average arterial pressure did not change, so that the HPR increased from 3.8 to 5.5 in the normotensive group, from 7.3 to 10.1 in the hypertensive group, and from 6.0 to 8.3 in the combined groups. These changes were significant statistically.

The changes in EHBF and HPR were not directly related to increases in pulse rate or to other signs and symptoms of poor circulatory adaptation to the upright posture (Table I). However, there was in general a correlation between the tendency of a subject to collapse and to have a low EHBF in the upright position. Thus, of the six subjects who fainted, four had an EHBF below 750 cc./min. during the upright period and another had it just after being tilted back horizontal. Although six of the ten subjects who had an upright EHBF below 750 cc./min. did not faint, three (Gio, She, Val) of them had the low flow only during the first six minutes after being tilted up, and on further standing had an EHBF above 750 cc./min.

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FIG. 3. CHART OF EHBF, ARTERIAL PRESSURE AND PULSE RATE IN A NORMOTENSIVE PATIENT (CAR)

At the heavy vertical line the left hand was immersed in ice water for one minute. Other notations as in Fig. 1.

Upon returning the subjects from the upright to the horizontal position the EHBF and HPR usually returned toward, to, or even beyond the control horizontal levels after varying periods of time. In some subjects the returns were prompt, in others they were delayed or incomplete, or occurred only after an initial overshoot beyond the previous horizontal values. In one hypertensive individual (Max) the post-tilt increases of EHBF and decreases of HPR were extreme and associated with a marked anxiety reaction that began with a severe headache.

Upon tilting the subjects back to the horizontal position the average values (Table II) changed as follows: EHBF rose from 1,070 to 1,312 in the normotensive group, from 960 to 1,417 in the hypertensive group, and from 1,004 to 1,372 in the combined groups, while the HPR decreased from 5.5 to 4.9, from 10.1 to 7.2, and from 8.3 to 6.2, respectively. Since the measurements during recovery showed greater variability than before tilting, the changes during this period, while significant for the combined and hypertensive groups, were not for the normotensive group considered separately.

Except in one patient (Sil), immersion of a

TABLE II

	(cc./n	EHBF (cc./min./1.73 sg. m.)			Mean§ arterial pressure (mm. Hg)			HPR (mm. Hg/cc./sec./1.73 sq. m.)		
	Horizontal (Control)	Upright	Horizontal (Recovery)	Horizontal (Control)	Upright	Horizontal (Recovery)	Horizontal (Control)	Upright	Horizontal (Recovery)	
Normotensives (n = 6) Mean Standard Error of Mean Mean Difference‡ Significance of Difference (P)	1,713 65 —	1,070 37 -642 < 0.01	$1,312 \\ 155 \\ +242 \\ 0.12$	98 3 —	97 2 -1 0.75	98 3 +1 0.81	3.8 0.1 —	5.5 0.6 +1.7 < 0.03	$ \begin{array}{r} 4.9 \\ 0.6 \\ -0.6 \\ 0.42 \end{array} $	
Hypertensives (n = 9) Mean Standard Error of Mean Mean Difference Significance of Difference (P)	1,357 97 	960 68 -397 < 0.01	1,417 172 +428 < 0.05	158 7 	157 7 -1 0.78	155 8 0 0.97	7.3 0.6 —	10.1 0.7 +2.8 < 0.01	7.2 0.7 -2.4 < 0.01	
Combined Groups (n = 15) Mean Standard Error of Mean Mean Difference Significance of Difference (P)	1,499 107 	1,004 61 -495 < 0.01	1,372 116 +348 < 0.01	134 9 —	133 9 -1 0.77	131 9 0 0.87	6.0 0.6 	8.3 0.8 +2.3 < 0.01	6.2 0.6 -1.6 < 0.01	

Mean values* of estimated hepatic blood flow (EHBF), arterial pressure and hepatic portal resistance (HPR) in relation to posture, with a statistical analysis of the significance of the differencest

* These data represent the group means calculated from the average values of EHBF, arterial pressure and HPR for each patient, shown in detail in Table I. Non-equilibrium observations (*i. e.*, those prior to four minutes after a change in posture, as well as those associated with a faint) were deleted from the calculations.

† The significance of the differences was calculated by Fisher's method for the significance of unique samples (12). presents the probability that a difference may be due to chance. Values of 0.05 or less (in **bold** type) denote a "signi-P represents the probability that a difference may be due to chance. ficant" difference, and 0.01 or less a "highly significant" one.

[‡] The differences refer to the change from the immediately preceding posture. Slight discrepancies between the mean changes from upright back to horizontal as compared to the mean values in these positions are due to the fact that observations were made on one hypertensive patient (Ric) during the control and upright periods, but not during recovery.

§ Average of the systolic and diastolic pressures.

hand in ice water for one minute caused slight or negligible effects upon EHBF, although it usually caused a temporary elevation of arterial pressure (Figure 3) and HPR. It was felt that this stimulus, despite its severity, was too brief in duration to produce regular effects upon EHBF; consequently, it was abandoned.

DISCUSSION

The results reported above confirm the impression gained from indirect evidence that active vasoconstriction occurs in splanchnic organs in addition to the kidneys when human subjects are tilted into the upright position. The decreases in EHBF found in the upright position can not be explained by changes in arteriovenous pressure gradient because the arterial pressure did not decrease proportionately and the atrial venous pressure is known not to increase in this position (7). Neither can the decreases in EHBF be attributed to other passive hydrostatic effects such as changes in blood volume (8) or intra-abdominal pressure (9). That the decreases in EHBF in the upright position are probably due to active vasoconstriction of sympathetic nervous origin has been indicated by repeating the studies of EHBF in some of the same subjects after splanchnicectomy (10).

No consistent differences in EHBF were found between the small group of hypertensive patients here reported and a larger group of normotensive subjects (11). The data indicate that the splanchnic circulation is not increased in hypertensive patients, but that calculated HPR is increased, reflecting the generalized vascular hypertonus usually regarded as characteristic of the disease. More evidence is being accumulated concerning these points by comparing the EHBF and HPR in the resting horizontal position in larger groups of hypertensive and normotensive subjects and will form the subject of a later report (11).

SUMMARY

Hepatic blood flow, as estimated by the bromsulfalein extraction method, decreased in eight normotensive and 12 hypertensive subjects after passive tilting into the upright (75°) position. It failed to change regularly in six subjects after immersion of a hand in ice water for one minute.

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