EFFECT OF INTRAVENOUS INFUSIONS OF ETHYL ALCOHOL ON ESTIMATED HEPATIC BLOOD FLOW IN MAN *

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The effect of ethyl alcohol on the splanchnic or liver blood flow has been a matter of debate. According to earlier investigations [Starling (1)] ethanol has little effect on the cardiovascular system, its influence being mainly confined to a dilatation of the vessels of the skin and of the mucous membranes. The investigation of Smythe, Heinemann and Bradley on dogs (2) supported this concept. However, Mendeloff (3) in studies on man observed a striking increase in the splanchnic blood flow during intravenous infusions of ethyl alcohol.

In this laboratory, metabolism of ethanol is now being studied. During these studies no effect of ethanol on the splanchnic blood flow could be found. The aim of this paper is to present these data.

MATERIAL AND METHODS

Six subjects were studied. Each was a healthy volunteer with no signs of cardiovascular or liver disease. In two, the procedure was repeated after several weeks had elapsed.

The technique was essentially that described by Bradley, Ingelfinger, Bradley and Curry (4). All studies were performed in the morning after an overnight fast. The subjects were recumbent. The sulfobromophthalein (BSP) solution was infused through a polythene catheter inserted a short distance into one of the antecubital veins; peripheral blood was obtained from a short polythene catheter in a brachial artery. The right hepatic vein was catheterized percutaneously through the femoral vein. The catheter used has been described by Ödman (5) as a modification of that of Gidlund (6).

The experiments were started with an estimation of the plasma volume. For this purpose 100 mg of BSP was given as a single injection and blood was sampled after 3, 5, 7 and 9 minutes from the artery for determination of the BSP space. An intravenous priming dose of 150 mg BSP was then given, followed by the sustaining infusion of BSP. This infusion was administered at a constant rate with a motor-driven syringe (7) so that approximately 2 ml of fluid was injected per minute. The bottle containing the infusion fluid was placed on an automatic balance enabling continuous control of the infused amount of fluid. As a rule approximately 3 mg BSP per minute per square meter body surface area was given. Sampling for analysis was not begun until after 30 minutes of infusion, to allow for equilibration between amount of infused and removed dye. Samples from the hepatic vein and the brachial artery were withdrawn simultaneously at 5 to 10 minute intervals. The basal splanchnic blood flow was determined over two periods of 5 to 10 minutes.

In 5 experiments a priming dose of 10 g ethanol [1] in 100 ml physiological saline was given intravenously during 5 minutes before the start of the sustaining infusion. A sustaining infusion ranging between 0.18 and 0.50 g of alcohol per minute was delivered in 3 to 5 ml saline. The ethanol infusion was continued, on the average, for 35 minutes. During the alcohol infusion, samples from the hepatic vein and the brachial artery were simultaneously drawn at 5 to 10 minute intervals. After finishing the ethanol infusion further sampling was made for 3 more determinations of the splanchnic blood flow.

The subjects did not show any sign of alcohol intoxication during the studies. There was no effect on pulse rate and blood pressure during the alcohol infusion except a slight tachycardia when the priming dose of ethanol was given.

Methods of analysis. Before sampling, the salt solution in the venous catheter was washed out by withdrawing 4 ml of blood, which was discarded. Samples were then obtained in heparinized tubes for analysis. The BSP determinations were made in duplicate in the Beckman DU spectrophotometer by using the principle of the second method described by Gaebler (8). The hematocrit was determined after spinning the blood in the Wifug hematocrit centrifuge at a rate of 3,000 rpm for 30 minutes. The estimated splanchnic blood flow (ESBF) and the BSP extraction ratio were calculated

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[1] The ethanol used was a redistilled product made from cellulose and distributed as a 96 per cent solution. It was manufactured by a Swedish state factory. The only contaminants are: methanol, less than 0.5 g per L; and acetaldehyde, less than 0.005 g per L.

TABLE I

Sulfobromophthalein (BSP) data and ethanol data in eight ethanol experiments

Case no.	Sex	Age	BSA	Time after start of infusion	Infused amount BSP	Arterial plasma BSP conc.	Percentage BSP extraction	BSP clearance	ESBF	Mean value	Infused amount ethyl alcohol	Arterial alcohol conc.	Hematocrit*
			m²		*mg/min*	*mg/100 ml*		*ml/min*	*ml/min*		*g/min*	*g/L*	%
53/59	M	39	2.07	Before	10.05	2.20†	65				0.177		41.0
				↓		2.21	60	450	1,220	1,200			
		Priming 10 g		0.0		2.32	59	410	1,170				
				4.0							Inf. in		
				13.5		2.38	58	410	1,200		↓		
				23.0		2.65	55	360	1,070				
				33.0		2.89	48	330	1,090				
				34.0	10.42	3.33	50	270	940	1,020	out		
				42.0		3.62	47	270	940				
				52.0	10.57	3.98	39	240	950				
				62.0		4.33	37	220	990				
54/65	M	40	2.00	Before	7.11	2.16	51				0.177		39.0
				↓		1.96	45	380	1,280	1,320			
		Priming 10 g		0.0		1.92	45	370	1,360				
				5.5							Inf. in		
				15.5		1.96	52	360	1,200		↓		
				26.5		1.91	52	380	1,190				
				36.0		1.87	50	380	1,230				
				37.0		1.81	52	400	1,280	1,240			
				46.0		1.75	51	410	1,300		out		
				56.0		1.73	54	410	1,280				
				66.0	↓	1.77	53	400	1,220				
57	M	31	1.93	Before	9.28	2.67	29				0.201		35.0
				↓		2.76	32	320	1,630	1,610		0.000	
				0.0		2.86	26	300	1,640			0.000	
				4.5				270	1,620		Inf. in		
				15.0		3.10	26	290	1,650		↓	0.046	
				25.5		3.17	27	240	1,460			0.067	
				35.5		3.49	24	230	1,380			0.077	
				36.0		3.77	27			1,420		0.095	
				46.0		4.03	28	210	1,210		out		
				56.5		4.30	19	200	1,320			0.044	
				66.0	↓	4.69	25	190	1,360			0.021	
												0.013	

* All the subjects were blood donors; this may explain the slightly subnormal hematocrit values.

† In Experiment 53/59 the arterial BSP plasma concentration rose with time. This rise does not significantly influence the calculated blood flow values (9, 10).

TABLE I—(*Continued*)

Case no.	Sex	Age	BSA	Time after start of infusion	Infused amount BSP	Arterial plasma BSP conc.	Percentage BSP extraction	BSP clearance	ESBF	Mean value	Infused amount ethyl alcohol	Arterial alcohol conc.	Hematocrit*
			m²		*mg/min*	*mg/100 ml*		*ml/min*	*ml/min*		*g/min*	*g/L*	%
58	M	21	1.86	Before	6.10	1.72	47	310	1,170		0.175		40.5
				↓		1.84	43	300	1,150	1,160		0.000	
						1.93	44					0.003	
				0.0				290	1,100		Inf. in		
				4.0		2.02	44	270	1,060		↓	0.061	
				14.0		2.18	41	250	1,090			0.078	
				24.0		2.37	35	240	1,140	1,090		0.083	
				34.0		2.46	37					0.112	
				35.0				240	1,200		out		
				44.0		2.52	31	220	1,110			0.076	
				54.5		2.70	34	200	960			0.020	
				64.5	↓	2.89	36					0.015	
59/53	M	39	2.07	Before	6.37	1.29	49	480	1,570		0.181		39
				↓		1.31	52	460	1,550	1,560		0.000	
						1.35	45					0.000	
		Priming 10 g		0.0				480	1,700		Inf. in		
				4.0		1.34	47	460	1,720		↓	0.410	
				14.5		1.38	41	470	1,890			0.250	
				25.0		1.35	41					0.240	
				36.0				450	1,670	1,650	out		
				37.5		1.42	46	440	1,560			0.210	
				46.0		1.44	47	420	1,520			0.180	
				56.0		1.49	45	400	1,480			0.150	
				66.5	↓	1.58	42					0.120	
60	M	24	1.98	Before	6.55	2.12	51	340	1,160				40.0
				↓		2.04	47	320	1,140	1,150		0.030	
						2.05	46					0.020	
		Priming 10 g		0.0							Inf. in 0.249		
				5.0		1.99	43	340	1,260		0.426	0.650	
				15.0		1.99	49	330	1,190		0.456	0.570	
				25.0		1.90	45	350	1,260	1,260	0.492	0.530	
				35.5		1.91	42	340	1,310			0.600	
				36.0				310	1,230		out		
				45.5		2.04	42	300	1,250			0.450	
				55.5		2.14	38	280	1,330			0.400	
				65.5	↓	2.25	33					0.400	

TABLE I—(*Continued*)

Case no.	Sex	Age	BSA	Time after start of infusion	Infused amount BSP	Arterial plasma BSP conc.	Percentage BSP extraction	BSP clearance	ESBF	Mean value	Infused amount ethyl alcohol	Arterial alcohol conc.	Hematocrit*
			m²		*mg/min*	*mg/100 ml*		*ml/min*	*ml/min*		*g/min*	*g/L*	%
61	M	27	2.07	Before	6.15	0.81	79				0.430		42.5
				↓		0.75	75	840	1,890	1,870		0.000	
						0.76	78	810	1,840			0.000	
		Priming 10 g		0.0							Inf. in		
				7.0		0.82	72	750	1,720		↓	0.650	
				17.0		0.86	72	720	1,700			0.500	
				27.5		0.90	71	690	1,660	1,430		0.620	
				38.0		1.00	80	620	1,410			0.590	
				39.0							out		
				48.5		1.16	74	530	1,190			0.440	
				59.0		1.21	79	510	1,150			0.460	
				69.0	↓	1.13	76	550	1,220			0.460	
65/54	M	40	2.00	Before	7.34	1.82†	54				0.473		37.5
				↓	2.72	1.77	50	430	1,320	1,410		0.000	
					6.53	1.18	48	460	1,490			0.000	
				0.0							Inf. in		
				3.0	8.07	1.50	59	340	1,010		↓	0.110	
				13.0		1.71	55	450	1,280			0.300	
				22.5		1.77	52	450	1,350			0.350	
				31.5		1.88	51	420	1,300	1,300		0.450	
				32.0							out		
				41.0		1.84	48	440	1,440			0.240	
				50.5		1.94	50	410	1,330			0.170	
				60.0	↓	2.01‡	50	390	1,260			0.220	

‡ Hemolysis.

from the following formulae:

$$\text{ESBF} = \frac{\text{removal} \times 100}{(p - h)\,(I - \text{Hct})};$$

$$\text{removal} = I \pm \frac{\Delta p \cdot \text{BSP space}}{100};$$

$$\text{BSP clearance} = \frac{\text{removal} \times 100}{p};$$

$$\text{extraction ratio} = \frac{(p - h)\,100}{p};$$

where I = infusion rate (milligrams per minute), p = arterial = peripheral plasma concentration (milligrams per 100 ml plasma), h = liver vein plasma concentration (milligrams per 100 ml plasma), Δp = change in p in milligrams per 100 ml plasma per minute, and Hct = hematocrit value in per cent.

Alcohol determination was made according to Bonnichsen and Lundgren (9).

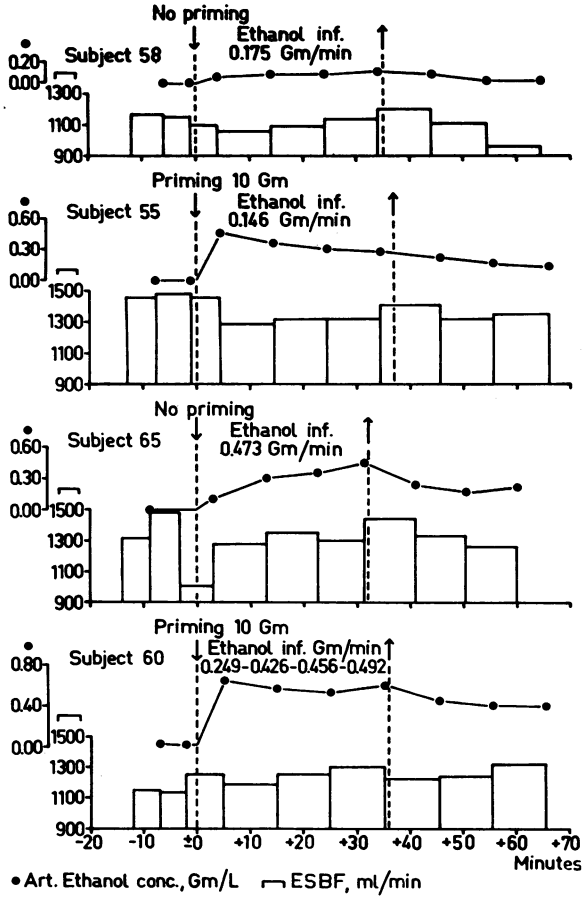

FIG. 1. THE ESTIMATED SPLANCHNIC BLOOD FLOW IN MILLILITERS PER MINUTE AND THE ETHANOL BLOOD CONCENTRATION IN GRAMS PER LITER IN FOUR OF EIGHT EXPERIMENTS.

RESULTS

The data from the eight studies are given in Table I. In Experiments 57, 58 and 65 no priming doses of ethanol were given, resulting in a slow increase in the blood concentration of ethanol. The infused amount of ethanol ranged between 0.18 and 0.50 g per minute. The arterial ethanol concentration in Experiments 53 and 54 was, for technical reasons, not obtained. In the remaining experiments the maximal concentration ranged between 0.10 and 0.65 g ethanol per L blood.

No effect of ethanol on the estimated splanchnic blood flow was observed in any of the subjects studied. Further, ethanol did not influence the BSP clearance. In Figure 1 four studies are illustrated.

DISCUSSION

The difference between our results and those of Mendeloff are difficult to explain. Essentially the same technique has been used in the two investigations. In Mendeloff's five experiments the blood concentration of ethanol ranged between 0.14 and 0.82 g ethanol per L, levels corresponding to our values of 0.10 to 0.65 g ethanol per L. However, our subjects were healthy volunteers while Mendeloff studied patients with gastric ulcer. Also, we gave no sedation while Mendeloff gave a subcutaneous injection of 60 mg phenobarbital sodium before the study. Such sedation would probably tend to depress the effect of ethanol on the splanchnic blood flow.

To find out if there is a different response to very low peripheral alcohol concentrations we kept the blood ethanol below 0.15 g per L in two experiments. The results in these experiments were the same as in those with blood alcohol concentrations above 0.15 g per L. There was also no effect on the ESBF in those experiments in which the blood concentration was raised from zero up to 0.65 g per L within five minutes (priming experiments).

In three experiments (nos. 53, 57 and 61) there was slight decrease in ESBF with time. As the same tendency was found in another study (11) without any drug, we suggest that this fall was a spontaneous change not due to ethanol.

SUMMARY

The effect of ethanol on the splanchnic blood flow was studied in eight experiments on six healthy volunteers using the sulfobromophthalein (BSP) method. No sedation was used. The peripheral ethanol concentration ranged between 0.10 and 0.65 g per L. There was no significant effect of the ethanol in any of the eight studies.

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