

Methoxamine and Cardiac Output in Nonanesthetized Man and During Spinal Anesthesia

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Methoxamine (approximately 0.2 mg./kg. body weight; range of total dose, 4 to 30 mg.) was given by intravenous infusion to two groups of patients: (1) 5 normotensive, nonanesthetized; and (2) 7 hypotensive under spinal anesthesia. In the nonanesthetized group, the criterion for dosage of methoxamine was elevation and maintenance of arterial blood pressure 25 per cent (± 10 per cent) above the resting level. In the hypotensive group, administration of vasopressor was guided by the elevation of arterial blood pressure to the pre-spinal control level. In the normotensive group, cardiac output and the heart rate were both significantly reduced, with variable changes in stroke volume. The vasopressor effect was associated with an elevated total peripheral resistance. In the hypotensive spinal group methoxamine caused variable changes in the cardiac output: increase or decrease in cardiac output depended on changes in stroke volume. The heart rate was generally reduced below the spinal level. The vasopressor effect was apparently due to the elevated total peripheral resistance and, in some instances, to an increased cardiac output. This increase in cardiac output depended mainly on increased stroke volume. These findings suggest that methoxamine in clinical dosage is not a myocardial depressant but a vasopressor capable of increasing the venous return to the heart which responds with increased stroke output.

METHOXAMINE,^o β -Hydroxy- β -(2, 5-dimethoxyphenyl) isopropylamine HCl, a potent sympathomimetic agent, exerts a primary influence upon the peripheral vascular bed causing an elevation of the systemic vascular resistance.^{1, 2} Some difference of opinion exists

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concerning its effect upon the heart. Several investigators reported that methoxamine was a cardiac depressant.³⁻⁶ Others found that it exerted no depressive influence upon myocardial contractile force.⁷

The value of methoxamine in the treatment of certain forms of hypotension has been questioned because of the reported reduction of cardiac output, decrease in rate of venous return and a possible negative inotropic effect upon the heart.^{4, 8}

This study was designed to determine the significance of the predominant peripheral action of methoxamine in relation to the other hemodynamic changes, particularly the cardiac output, in patients with induced hypotension due to spinal anesthesia as compared with the changes in nonanesthetized subjects. During spinal anesthesia methoxamine is usually administered as a single dose to elevate the arterial blood pressure because it is considered to be a long-acting agent. The evaluation of the hemodynamic effects of methoxamine in this study was thus based upon the response to a single dose which elevated and maintained the arterial blood pressure at a desired level.

Methods

Twelve patients from 25 to 70 years of age, without apparent cardiac or pulmonary disease, were studied prior to operation. Each patient was placed in a comfortable supine position on an operating table after 12 hours of fasting without premedication. The following measurements and calculations were made: heart rate, systemic arterial blood pressure, cardiac output, stroke volume, total peripheral resistance and left ventricular work. Cardiac output was determined by an indicator dilution technique using indocyanine green dye.^{9, 10, 11} The dye was injected into an antecubital vein and blood was simultaneously withdrawn

by a constant flow system (0.9 ml./second) from a brachial artery through the cuvette of a Colson densitometer (Model 103-IR). The methods for recording arterial blood pressure, lead 2 of the electrocardiogram and for calculating total peripheral resistance and left ventricular work have been previously described.^{12, 13, 14}

Control measurements were made after a spinal catheter and venous and indwelling arterial needles were inserted, and the patient had been quiet for at least 30 minutes. After control observations, methoxamine was administered to two groups: (1) 5 normotensive nonanesthetized subjects and (2) 7 subjects during the hypotensive state of spinal anesthesia.

The level of the arterial blood pressure served as a guide for the total dosage of methoxamine to be administered. Thus, the total amount of methoxamine varied from patient to patient. The directional change of the arterial blood pressure revealing the degree of the vasopressor effect was maintained at a constant level for all subjects studied: (1) 25 per cent (± 10 per cent) above the control levels for the nonanesthetized group of patients; and (2) the correction of the hypotension with a return of the blood pressure to the pre-spinal level for the anesthetized patients.

Methoxamine was administered in 0.03 per cent solution in normal saline, and infused at the rate of 5-10 ml. per minute. The beginning of the infusion of methoxamine was designated as the "zero time." Hemodynamic determinations were made periodically following termination of the infusion. The total dosage of methoxamine ranged from 4 to 30 mg. (average: 0.2 mg./kg. body weight).

Nonanesthetized Subjects. Immediately after the control observations, methoxamine was infused to elevate the arterial blood pressure 25 per cent (± 10 per cent) above the resting level. The elevation of the blood pressure served as a criterion for the dosage administered.

Spinal Anesthesia. The catheter spinal anesthesia technique was described in detail in a previous publication.¹⁴ Pontocaine (0.3 per cent solution in 10 per cent dextrose) was given in divided doses until the mean arterial blood pressure fell to 25 per cent (± 10 per

cent) below the resting "normotensive" level.¹⁴ The total dosage of pontocaine varied from 6 to 15 mg. The sensory level of anesthesia to pin prick was tested periodically and ranged from third to tenth thoracic level throughout the experiment. When the hemodynamic response to spinal anesthesia was stabilized, as indicated by no further changes in arterial blood pressure and heart rate, measurements of cardiac output and other parameters were repeated during this "hypotensive" initial level.¹⁴ Methoxamine was then administered in the same manner as in the nonanesthetized subject to restore the arterial blood pressure to its pre-spinal "normotensive" initial level. After the stable state was obtained, as indicated by no further fluctuation of arterial blood pressure, the infusion was stopped.

P values were obtained by means of the *t* test. The *sign test*¹⁵ was used to determine the significance of the directional changes in cardiac output following administration of methoxamine to the nonanesthetized subjects.

Results

Pertinent hemodynamic data are summarized in table 1 (nonanesthetized subjects) and table 2 (anesthetized subjects).

NONANESTHETIZED SUBJECTS

Cardiac Index. Administration of methoxamine to 5 nonanesthetized subjects resulted in a decrease of cardiac index in 17 of 18 measurements. The mean value of the cardiac index during the resting period was 3.01 ± 0.54 liters/minute/m.² within the normal variability. The decrease of cardiac index following the administration of methoxamine ranged from 0.18 to 0.84 liter/minute/m.². The mean percentage change was -15.8 per cent. However, in one instance the cardiac index (subject E. P.) was increased ($+0.3$ liter/minute/m.²) (table 1). The values for cardiac indices in repeated determinations within 10 minutes in 3 subjects varied by 4.2 per cent from the mean values. Changes in cardiac index in 17 of 18 observations were greater than 4.2 per cent and, therefore, were considered significant. Furthermore, analysis of the directional changes in cardiac index by means of a *sign test*¹⁵ revealed that there were 17 cases of reduction

in cardiac index and one increase; the hypothesis that methoxamine does not cause a significant directional change in cardiac output is therefore untenable ($P < 0.001$).

Heart Rate. The mean heart rate among the five nonanesthetized subjects during the resting period was 80 ± 4 beats/minute. Administration of methoxamine resulted in a reduction of heart rate in all instances. Production of bradycardia was statistically significant ($P < 0.01$), ranging from -8 to -42 beats/minute, the effect lasting more than an hour (table 1).

Stroke Volume Index. The mean stroke volume index among the 5 nonanesthetized subjects prior to and after the administration of methoxamine was 37.7 ± 1.8 and $37.4 \pm$

1.2 ml./beat/ m^2 , respectively. The average change in stroke volume index was not significant ($P > 0.5$) (table 1).

Mean Arterial Blood Pressure. Mean arterial blood pressure was 102 ± 6.2 mm. of mercury in the nonanesthetized subjects. Following the administration of methoxamine, the mean arterial blood pressure was always increased (range: $+3$ to $+39$ mm. of mercury) (table 1). The increases in the arterial blood pressure were significant ($P < 0.01$) at any time interval within one hour after the administration of the drug and were related to the increase of total peripheral resistance in all subjects.

Total Peripheral Resistance. The mean total peripheral resistance in nonanesthetized

TABLE 1. Hemodynamic Data Before and After Administration of Methoxamine in Nonanesthetized Subjects

Patient	Age (yrs.)	Time (min.)	Cardiac Index (l./min./ m^2)	Heart Rate (beats/min.)	Stroke Vol. Index (ml./beat/ m^2)	Mean Art. Pressure (mm. Hg)	T.P.R. ($\frac{\text{dynes-sec.}}{\text{cm.}^2}$)	Left Vent. Work (kg.-m./min.)	
M. M.	43	-14	2.61	72	36	118	2.20	6.57	
		+7 +51	2.15 2.43	57 69	38 35	142 125	3.34 2.61	6.51 6.32	
E. P.	52	-32	2.52	76	33	90	1.78	4.91	
		+5 +15 +32	2.82 2.00 2.28	64 72 68	44 28 34	103 90 90	1.82 2.25 1.97	6.28 3.89 4.44	
N. M.	39	-10	3.34	93	36	112	1.53	8.84	
		+9 +21 +43 +57	2.51 2.55 2.54 2.42	69 66 78 72	36 39 33 34	130 125 115 125	2.37 2.24 2.07 2.22	7.70 7.51 6.89 7.14	
J. O.	35	-7 -4	2.80 2.77	68 70	41 40	88 83	1.61 1.53	5.19 4.85	
		+13 +22 +39 +44	1.98 2.57 2.12 1.93	63 63 54 62	31 41 39 31	105 122 88 95	2.72 2.43 2.13 2.52	4.37 6.61 3.92 3.86	
M. N.	40	-8	3.79	88	43	103	1.37	8.37	
		+12 +25 +42 +55 +64	3.08 3.38 3.41 3.42 3.70	70 86 86 84 78	44 39 40 41 47	135 120 117 118 117	2.20 1.78 1.73 1.74 1.59	8.94 8.71 8.55 8.65 9.30	

TABLE 2. Hemodynamic Data Before and After the Administration of Methoxamine During Spinal Anesthesia

Patient	Age (yrs.)	Time (min.)	Cardiac Index (l./min./m. ²)	Heart Rate (beats/min.)	Stroke Vol. Index (ml./beat/m. ²)	Mean Art. Pressure (mm. Hg)	T.P.R. (dynes-sec. cm. ²)	Left Vent. Work (kg.-m./min.)
P. B.	70	C-41	2.45	69	35	140	2.74	7.29
		S-1	1.13	54	19	56	3.03	1.75
		M+3	1.42	57	25	203	6.97	6.35
		M+19	2.18	52	42	160	3.58	7.73
		M+187	2.35	63	37	125	2.57	6.51
J. C.	43	C-25	3.12	126	25	105	1.56	7.60
		S-13	1.94	100	19	85	2.03	3.83
		S-8	1.82	84	22	67	1.71	2.82
		S-3	1.93	82	24	67	1.61	3.00
		M+6	2.50	70	36	115	2.14	6.68
		M+12	2.21	76	29	100	2.10	5.14
		M+32	2.37	76	31	110	2.15	6.06
		M+41	2.43	78	31	105	2.00	5.93
		M+45	2.26	78	29	105	2.16	5.50
		S. M.	43	C-77	2.04	72	28	102
S-11	1.36			66	21	73	3.18	1.81
M+12	1.77			56	32	103	3.44	3.33
M+16	1.70			48	35	127	4.43	3.93
M+23	2.09			46	45	120	3.40	4.56
M+28	1.98			56	35	122	3.65	4.40
M. B.	38	C-26	3.27	56	59	75	1.20	5.04
		S-4	2.80	48	58	47	0.88	2.70
		M+10	2.60	46	56	70	1.42	3.73
		M+20	2.29	44	52	77	1.77	3.62
		M+40	2.41	52	46	78	1.70	3.86
		M+59	1.94	52	37	75	2.04	2.98
F. P.	25	C-07	4.30	81	53	105	1.18	10.11
		S-14	3.29	76	43	90	1.32	6.64
		M+7	3.46	86	40	116	1.62	8.98
		M+18	3.62	80	45	115	1.53	9.34
		M+27	2.87	74	39	115	1.93	7.39
		M+37	2.28	72	32	97	2.05	4.96
M. N.	42	C-23	1.88	60	31	105	2.44	4.87
		S-4	2.28	68	34	65	1.24	3.66
		M+5	1.30	36	36	122	4.10	3.91
		M+12	1.78	48	37	100	2.45	4.40
		M+22	1.34	50	27	98	3.19	3.24
		M+32	1.79	52	34	92	2.24	4.07
M+49	2.13	52	41	92	1.89	4.83		

TABLE 2. (Continued)

Patient	Age (yrs.)	Time (min.)	Cardiac Index (l./min./m. ²)	Heart Rate (beats/min.)	Stroke Vol. Index (ml./beat/m. ²)	Mean Art. Pressure (mm. Hg)	T.P.R. (dynes-sec./cm. ²)	Left Vent. Work (kg.-m./min.)
R. S.	41	C-47	4.15	93	45	95	1.18	8.25
		S-20	3.28	96	34	82	1.29	5.63
		S-10	3.33	87	38	90	1.40	6.26
		S-1	3.10	84	37	90	1.50	5.83
		M+21	2.63	66	40	88	1.72	4.85
		M+37	2.81	78	36	92	1.69	5.41
		M+48	2.57	72	36	105	2.11	5.65
		M+58	3.00	75	40	100	1.72	6.27
		M+68	2.10	60	35	120	2.94	5.27
		M+78	2.30	66	35	95	2.13	4.57
		M+86	2.94	72	41	100	1.76	6.14
		M+97	2.44	72	34	100	2.11	5.10

subjects was 1.6 ± 0.1 absolute units. Following administration of methoxamine, the total peripheral resistance was increased in all instances (range: +0.1 to +0.2 absolute units) (table 1). These increases were significant ($P < 0.02$).

Left Ventricular Work. In the nonanesthetized subjects, the mean left ventricular work was 6.5 ± 1.0 kg.-m./minute. Following the administration of methoxamine, there were variable changes in left ventricular work ($P > 0.2$) (range: +2.0 to -1.9 kg.-m./minute) (table 1).

ANESTHETIZED SUBJECTS

Cardiac Index. In the hypotensive group, after spinal anesthesia, the mean value of the cardiac index dropped from a control resting value of 3.03 ± 0.37 liters/minute/m.², to 2.39 ± 0.81 liters/minute/m.² in all but one subject ($P < 0.05$). In the seventh subject the cardiac index was increased during spinal anesthesia with an accompanying increase in heart rate (M. N. in table 2). Repeated determinations of cardiac index were made in 2 patients during spinal anesthesia. In one patient (J. C.) three cardiac index values determined within 15 minutes ranged from 1.82 to 1.94 liters/minute/m.² (pre-spinal control: 3.12); and in the other patient (R. S.) three cardiac output values obtained within 30 minutes varied from 3.10 to 3.33 liters/minute/m.² (pre-spinal control: 4.15) (table 2). These

results indicate that the values of the cardiac output were all lowered from the pre-spinal control level and had become stabilized under spinal anesthesia.

In 3 subjects with hypotension, the administration of methoxamine resulted in a decrease in cardiac index (M. B., M. N. and R. S.), that is, the cardiac index fell to a level lower than that during the spinal anesthesia prior to the administration of methoxamine. In the other 3 patients the cardiac index increased (P. B., J. C. and S. M.). The remaining one patient (F. P.) showed some increase in the cardiac index during the first 20-minute period following the administration of methoxamine, but from 25 minutes on, the cardiac index fell below the spinal level. Figure 1 demonstrates these variable changes in cardiac index in all 7 patients in reference to their initial, pre-spinal control values, respectively.

The two patterns of hemodynamic response are illustrated in figures 2 and 3 where the hemodynamic changes are plotted against time in two cases. Figures 2A and 2B illustrate an experiment (M. B.) where cardiac output was further reduced from the hypotensive level, 14 per cent decrease from the pre-spinal control value. In twenty minutes following the administration of methoxamine there was an additional 10 per cent reduction of cardiac output and in sixty minutes there was a 20 per cent further reduction (figures 2A and 2B;

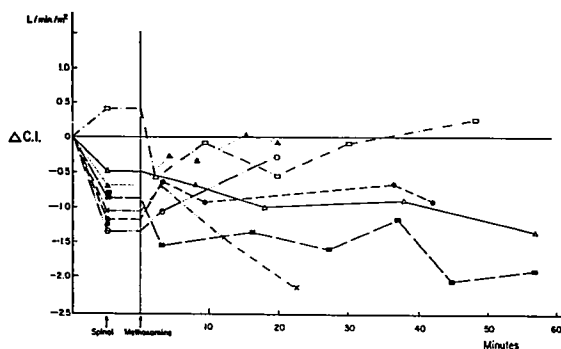
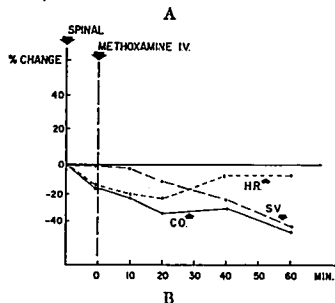
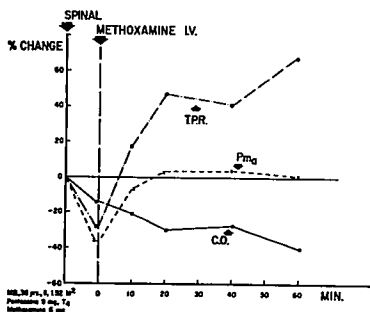


FIG. 1. Line graph of 7 separate experiments. Changes (triangle) of the index values are plotted against time during the control, pre-spinal state, before and after the administration of methoxamine during spinal anesthesia. The arrow above "methoxamine" indicates the beginning of the infusion of the drug.



FIGS. 2A and 2B. Hemodynamic changes of a single experiment during spinal anesthesia. 2A (above): The elevation of the arterial blood pressure after methoxamine is due to the sustained increase of the total peripheral resistance. 2B (below): The reduction of the cardiac output is due to the initial decrease in the heart rate and subsequent decrease of stroke volume. O time on the vertical axis marks the beginning of the intravenous infusion of methoxamine. O, as related to percentage changes, indicates the pre-spinal level of control.

M. B. in table 2). In contrast, Figures 3A and 3B (P. B. in table 2) demonstrate a 54 per cent reduction of the cardiac output during spinal anesthesia, but a return of cardiac output to the normotensive range twenty minutes after the administration of methoxamine.

Heart Rate. Spinal anesthesia in 7 subjects caused a reduction of heart rate in 9 of 11 instances (table 2). In only one of 7 patients was there a definite increase in the heart rate, all the other 6 patients had a reduced heart rate during spinal anesthesia. The mean heart rate before and during spinal anesthesia was 80 ± 9 and 69 ± 7 beats/minute, respectively ($P > 0.1$).

Following the administration of methoxamine, there were 6 instances of increase in heart rate (range: +3 to +9 beats/minute), and all the remaining 27 instances showed a further reduction of heart rate (range: -2 to -32 beats/minute) (table 2). Only in 2 (P. B. and F. P.) (table 2) of 7 patients was there a slight increase in heart rate; the other 5 subjects all had further drop of heart rate. This reduction in heart rate following the administration of methoxamine during spinal anesthesia is statistically significant ($P < 0.05$).

Stroke Volume Index. The mean stroke volume index during spinal anesthesia dropped from 36.6 ± 6 ml./beat/m.² to 33.0 ± 6 ml./beat/m.². Following the administration of methoxamine there were variable changes in the stroke volume index (range: -21 to +24 ml./beat/m.²). These changes were not statistically significant ($P > 0.1$). Figure 2B

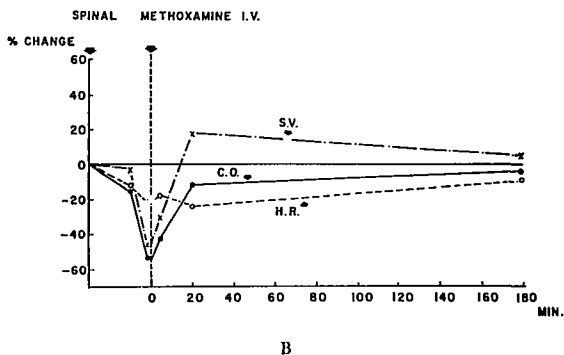
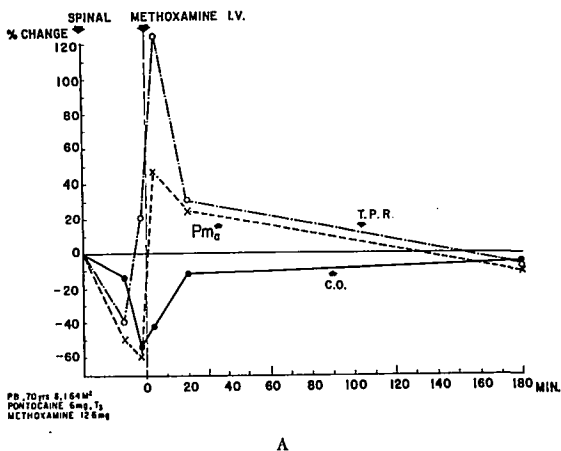
shows an instance of progressive reduction of stroke volume following the administration of methoxamine. This occurred in a patient (M. B.) with a high stroke volume index (59 ml./beat/m.²) at the pre-spinal level, and it was not reduced during spinal anesthesia. In the two other experiments (F. P. and R. S.), the stroke volume index was relatively high (S.V.I. = 59, 53 and 45 ml./beat/m.², respectively) at the pre-spinal level. These 3 subjects had either a reduced or unaltered stroke volume following the administration of methoxamine.

This, however, only represents one pattern

of response to methoxamine and the opposite pattern of response is illustrated by figure 3B where the stroke volume index increased with methoxamine (+ 20 per cent above the pre-spinal, normotensive level and + 70 per cent above the spinal, hypotensive level). All 4 patients (P. B., S. M., J. C. and M. N.) with such an increase in stroke volume demonstrated relatively low stroke volumes at the start (pre-spinal S.V.I. = 35, 28, 25, and 31 ml./beat/m.², respectively).

Mean Arterial Blood Pressure. Among 7 subjects during spinal anesthesia, there was a significant drop in mean arterial blood

FIGS. 3A and 3B. Hemodynamic changes in a single experiment during spinal anesthesia. Figure 3A (above) shows that the arterial blood pressure increase following methoxamine is due to the increased total peripheral resistance and cardiac output. Figure 3B (below) illustrates that the increase in cardiac output is primarily due to the increase in stroke volume.



pressure from an average of 104 ± 6.3 mm. to 63.6 ± 6 mm. of mercury ($P < 0.01$). Methoxamine administered during the hypotensive period always caused an increase of the mean arterial blood pressure (range of increase: +7 to +69 mm. of mercury). Such an increase in arterial blood pressure was significant at any time interval after the termination of administration of the drug ($P < 0.01$).

Figure 2A illustrates this vasopressor effect of methoxamine. The arterial blood pressure was elevated to the pre-spinal, normotensive level in 10-20 minutes following the administration of methoxamine. Figure 3A shows a temporary, transient overshoot of mean arterial blood pressure followed by a prolonged normotensive period of more than one hour.

Total Peripheral Resistance. Among the 7 subjects studied during spinal anesthesia, there were five instances of increased total peripheral resistance (range: +0.1 to +0.3 abs. units) and two with reduced total peripheral resistance (range: -0.3 to -1.2 abs. units) ($P > 0.5$). Following the administration of methoxamine there was consistently an increase of total peripheral resistance (in reference to the values during the spinal anesthesia before the administration of the drug) in 32 of 33 instances ($P < 0.01$) (table 2).

Figure 2A shows a marked progressive elevation of total peripheral resistance lasting more than one hour following the administration of methoxamine. Figure 3A illustrates a striking increase in total peripheral resistance; immediately following the administration of methoxamine there was an increase in total peripheral resistance of +200 per cent in reference to the hypotensive level and over 100 per cent in relation to the resting, pre-spinal level.

Left Ventricular Work. During spinal anesthesia there was always a reduction in left ventricular work (mean reduction: 2.2 ± 0.7 kg.-m./minute ($P < 0.01$)). Methoxamine generally increased left ventricular work (range: +0.3 to 6.0 kg.-m./minute); in only 2 instances was the left ventricular work reduced (-0.4 and -1.7 kg.-m./minute). These increases in left ventricular work were significant at 3 and 15 minute intervals ($P < 0.02$ and < 0.05 , respectively).

Discussion

The hemodynamic response to the administration of methoxamine for the treatment of hypotension in patients under spinal anesthesia differed from the response observed in non-anesthetized, normotensive subjects. Cardiac output was significantly reduced and associated with a bradycardia following the administration of methoxamine to normotensive non-anesthetized subjects. These findings in the normal subjects are in agreement with the results reported by others.^{2,3,4,10} In contrast, during spinal anesthesia, changes in cardiac output were inconsistent and varied from patient to patient after administration of methoxamine. Three of the 7 patients studied had reduced cardiac output and the other three showed an increase. These changes were not statistically significant. In general, two different patterns of hemodynamic response can be recognized: one is a further reduction of the cardiac output during spinal anesthesia associated with reduced stroke volume. The other pattern is an increased cardiac output due to an increased stroke volume.

The significant observation is that the circulatory response to methoxamine in the non-anesthetized normotensive subjects is unique and straight-forward in contrast to the variable directional change of the cardiac output in the hypotensive patients under spinal anesthesia. Since the change in the cardiac output depends on so many factors in the body, in the hypotensive state the situation may be further complicated by the fact that all the responses of the cardiovascular tissues could be altered and different from the normotensive state. The following possibilities may account for the difference in response during the hypotensive state under spinal anesthesia.

The pressor effect of methoxamine is believed to be primarily due to its stimulating effect upon the alpha-adrenergic receptors in the peripheral vascular bed.¹⁷ It is reported that methoxamine does not evoke the liberation of the catecholamines from the storage portion in the cardiovascular tissues.^{12, 13} However, it has been shown that during hypotensive episodes, the circulatory and the storage portion of catecholamines are increased.²⁰ Recent investigation in this laboratory has not

found substantial increase in the plasma catecholamine during spinal anesthesia.²¹ The sensitivity of the smooth muscle of the blood vessels or the alpha-adrenergic receptors to methoxamine might well be altered during the hypotensive state of spinal anesthesia, thereby producing circulatory effects different from those during the normotensive state.

Another possibility is the vasoconstrictive effect of methoxamine, which has been shown to increase the peripheral venous pressure, although it has little effect upon venous tone in the forearm.²² During the hypotensive state of spinal anesthesia, veins may react differently from the normotensive state. The hypotension during spinal anesthesia is believed to be due to the reduction of total peripheral resistance in addition to the decrease in cardiac output as a result of pooling of blood in the peripheral vascular bed. The result of this study shows that in this hypotensive state methoxamine is able to increase the venous return to the heart, hence, increasing the stroke output.

It must be realized that the cardiac output does not necessarily reflect the actual status of the contractile mechanism.^{23, 24} Changes in cardiac output depend upon many factors, including the magnitude of venous return, heart rate, effective ventricular filling pressure in addition to the inotropic state of the myocardium and peripheral vascular resistance. The direction of the changes in these factors may increase, decrease or show no change of the cardiac output in the presence of an altered cardiac performance. The reduction of cardiac output as demonstrated by the present study in the nonanesthetized subjects and in the hypotensive subjects (3 out of 7) does not implicate any deleterious effects of methoxamine upon the heart.

There is sufficient evidence to support the contention that methoxamine in therapeutic dosage exerts no depressive effect upon the myocardium.^{7, 25, 26} Recently, by applying a miniature square-wave electromagnetic flowmeter to the intact coronary artery of a dog, methoxamine has been shown by Marston, Barefoot and Spencer²⁷ to increase the coronary blood flow. Duke *et al.*²⁸ recently reported some increase of stroke volume during

and after the intravenous infusion of methoxamine to a series of normal subjects. There was no significant change in the cardiac output with bradycardia. There was no evidence of ventricular failure, in the face of increased systemic vascular resistance. They believed the increase of the stroke volume was due to lengthened diastolic filling period, increased filling pressure and elevated "central" blood volume, and the effects of the drug appeared to be dose dependent. Their findings, we believe, would support the concept that methoxamine, within the range of clinical dosages, exerts no deleterious effect upon the heart and that the myocardial response to the increase of the venous return is adequate.

Summary

The hemodynamic effects of methoxamine were studied in 12 human subjects divided into two series: (1) normotensive, nonanesthetized and (2) hypotensive under spinal anesthesia.

Invariably, methoxamine reduced the cardiac output and heart rate in nonanesthetized subjects. Changes in the stroke volume, however, were variable. The vasopressor effect was associated with the elevated total peripheral resistance.

Changes in cardiac output varied from patient to patient following the administration of methoxamine during the hypotensive state under spinal anesthesia. The changes in the stroke volume paralleled the changes in cardiac output, and, in most instances, the heart rate was reduced. The vasopressor effect was generally due to the elevated total peripheral resistance although in certain cases there was also an increase in cardiac output. The increase in stroke output is presumably due to the augmented venous return to the heart indicating an adequate myocardial response.

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