Circulatory reflexes in myocardial infarction

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The Valsalva manoeuvre was used to examine circulatory reflexes in 22 patients with acute myocardial infarction. Four patients had the 'square wave' response of cardiac failure and two responded normally to the manoeuvre. In the remaining 18 patients there was a 20 per cent or more fall in pulse pressure during the manoeuvre, but no ensuing rise in diastolic pressure, implying impairment of vasoconstriction. This impairment cannot be explained by acidosis, hypocapnia, or arterial hypoxaemia but may be explained by reflex inhibition of vasoconstriction. This abnormal response has important implications when transporting patients; furthermore, it could explain the rapid deterioration sometimes seen in patients with arrhythmias.

Reflexes arising from the heart could impair the normal response of the peripheral circulation to a reduced cardiac output and could explain the frequently observed failure of systemic vasoconstriction to compensate adequately for the fall in cardiac output after myocardial infarction (Smith *et al.*, 1954; Lee, 1957; Thomas *et al.*, 1966; Ramo *et al.*, 1970). This concept was not confirmed by earlier animal experiments (Levy and Frankel, 1953; Wegria *et al.*, 1954), but more recent ones have shown that reflexes arising in infarcted myocardium inhibit reflex vasoconstriction (Costantin, 1963; Kolatat *et al.*, 1967; Toubes and Brody, 1970). It is an attractive hypothesis to suggest that similar impairment of vasoconstriction occurs in man, but the general anaesthesia, the difference in autonomic responses in animals, and the technique of inducing myocardial infarction in these animal experiments are such that these observations may not be entirely applicable to man. However, there is clinical evidence to support the idea of an autonomic disturbance after myocardial infarction in man (Webb *et al.*, 1972). The present study has attempted to seek evidence of impairment of circulatory reflexes in man after myocardial infarction. The Valsalva manoeuvre was used for this purpose as it could be easily applied at the bedside and has been used successfully without harm to the patient to detect heart failure in angina (Elisberg, 1963) and in myocardial infarction (Lee, 1957).

In normal subjects when the intrathoracic pressure is raised during the Valsalva manoeuvre there is a prompt fall in pulse pressure, and as a

consequence of stimulation of the baroreceptor reflex there is vasoconstriction and an increase in pulse rate. Persistence of vasoconstriction for a few moments after the return of intrathoracic pressure to normal at the finish of the manoeuvre coupled with an increase in venous return results in an increase in diastolic pressure above control levels—the so-called 'overshoot' phase. Two types of abnormal response have been recognised: (1) the 'square wave' response of cardiac failure in which there is no fall in pulse pressure and no ensuing rise in diastolic pressure during the overshoot phase, and (2) an abnormal response where, despite a fall in pulse pressure during the manoeuvre, there is no reflex vasoconstriction, and as a consequence no increase in diastolic pressure during the overshoot phase. The impairment of the baroreceptor reflex in this latter situation also results in either no, or only a small, increase in heart rate during the manoeuvre.

Patients and methods

Acute myocardial infarction was diagnosed in 22 men aged between 42 and 69 years (mean = 57 years) on the basis of a characteristic history, unequivocal electrocardiographic evidence, and a subsequent diagnostic rise in either serum creatine phosphokinase or hydroxybutyric dehydrogenase. Patients with chronic respiratory disease, previous cardiac failure, or those who had received morphine in the previous four hours, were excluded as these factors may influence the response to the Valsalva manoeuvre. The nature and purpose of the study was carefully explained to each patient and their consent

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obtained. An 18 gauge 5 cm 'teflon' catheter ('Longdwell' Becton, Dickinson Inc.) was inserted percutaneously under local anaesthesia into a brachial artery and connected to a pressure transducer connected to a preamplifier and a direct writing recorder (Devices Instrument Ltd.). The zero level was adjusted to 10 cm below the sternal angle with the patient resting comfortably with the shoulders raised to a semi-recumbent position. Patients were shown how to carry out the manoeuvre, and after several trial attempts, with intervening rest periods, the intra-arterial pressure was recorded continuously before, during, and after the manoeuvre. The Valsalva manoeuvre was performed by supporting a 40-mm column of mercury for as long as possible and in all cases for at least 10 seconds. The following measurements were made from the recording: (1) systolic and diastolic pressures and heart rate in the control period, (2) the minimum pulse pressure during the manoeuvre, (3) the maximum diastolic pressure immediately after the manoeuvre, and (4) the maximum increase in heart rate during the manoeuvre. From the measurements the following were calculated: (1) percentage decrease in pulse pressure during the manoeuvre, (2) percentage increase in diastolic pressure after the manoeuvre, (3) the percentage increase in heart rate during the manoeuvre, (4) the ratio of the percentage increase in heart rate to the

percentage decrease in pulse pressure, and (5) the ratio of the percentage increase in diastolic pressure after the manoeuvre to the percentage decrease in pulse pressure.

Arterial blood was analysed in 20 patients for pH, carbon dioxide, and oxygen tension using a Radiometer blood gas and pH analyser (Model 27).

Results

Individual and mean results are shown in the Table. Four patients (Cases 3, 10, 11, 13) had a less than 20 per cent reduction in pulse pressure and the configuration of their response corresponded to the 'square wave' response of cardiac failure (Sharpey-Schafer, 1955). The remaining 18 showed their ability to perform the manoeuvre by a prompt reduction of at least 20 per cent in pulse pressure and 16 of them achieved a reduction of over 40 per cent. Despite this substantial fall in pulse pressure during the manoeuvre, only 2 had a normal rise in diastolic pressure during the overshoot phase when compared with the data compiled in 360 normal subjects by Sharpey-Schafer and Taylor (1960). Fifteen patients had a less than 15 per cent rise in diastolic pressure during the overshoot phase and in 7 patients there was a change of only 2 mmHg or less (Fig. 1). The majority (89%) had evidence of an impaired rise in diastolic pressure during the

Table Results of Valsalva manoeuvre in individual patients

Case No.	Age (y)	Systolic BP	Diastolic BP	Control pulse pressure	Valsalva pulse pressure	Per cent reduction in pulse pressure	Diastolic pressure after Valsalva	Per cent increase in diastolic pressure	Control HR	Per cent increase in HR	[H ⁺] (nmol/l)	Pco ₂	Po ₂
1	61	97	48	49	21	57	58	21	106	0	32	33	60
2	59	136	82	54	18	67	92	12	94	33	36	31	63
3	40	84	60	24	20	17	56	-7	76	20	—	—	—
4	64	154	85	69	37	46	86	1	72	0	35	27	80
5	66	162	87	75	58	23	100	15	104	0	37	38	56
6	45	129	94	35	17	51	98	4	63	11	31	23	90
7	42	124	72	52	22	58	89	17	60	20	41	34	76
8	69	122	76	46	11	76	80	5	72	10	33	32	63
9	49	100	55	45	16	64	100	82	112	0	40	34	66
10	65	113	68	45	40	11	67	-1	78	0	39	29	70
11	54	175	97	78	75	4	100	3	60	12	39	35	79
12	53	140	81	59	10	83	87	7	69	20	39	34	71
13	57	181	100	81	66	18	109	9	64	9	—	—	—
14	59	145	85	60	18	70	97	14	116	30	39	33	72
15	62	98	57	41	24	41	55	-4	52	15	35	31	62
16	62	125	85	40	14	65	100	18	80	25	39	34	80
17	58	102	55	47	15	68	64	16	69	30	50	42	71
18	57	75	48	27	12	55	48	0	100	0	45	40	71
19	55	165	80	85	19	78	102	28	72	27	45	37	88
20	63	81	50	31	18	42	49	-2	88	20	37	33	55
21	60	115	65	50	39	22	66	1	68	0	42	37	53
22	57	146	92	54	25	54	92	0	108	17	40	30	88
Mean	57.1	125.9	73.7	52.1	27.0	48.7	81.6	11.9	81.0	13.6	38.7	33.3	70.7
SEM	1.62	6.52	3.56	3.65	3.88	4.99	4.22	3.75	4.09	2.43	0.98	0.94	2.37

Pressure measurements are given in mmHg.

overshoot phase. There was no correlation between the magnitude of the diastolic overshoot and (a) the site of myocardial infarction, (b) the arterial pressure, (c) hydrogen ion concentration, (d) arterial carbon dioxide tension, or (e) arterial oxygen tension.

In addition to reflex vasoconstriction, the Valsalva manoeuvre results in an increase in heart rate in normal subjects during the manoeuvre. Five of the 18 patients in whom pulse pressure fell during the manoeuvre had a 20 per cent or more increase in heart rate and could be regarded as having a normal response, but in the remaining 13 (72%) the response was impaired (Fig. 2). In general those with the smallest rise in diastolic pressure in the overshoot phase were the same patients as had the least rise in heart rate during the manoeuvre but there was a pronounced disparity in 4 patients (Cases 3, 12, 20, and 22). These 4 patients had a rise of less than 10 per cent in diastolic pressure yet heart rate increased by up to 20 per cent during the manoeuvre.

Arterial carbon dioxide tension was below 35 mmHg in 14 (70%) but hydrogen ion concentration was within the normal range. Ten patients

had an arterial oxygen tension below 70 mmHg. None of these variables had a statistical correlation with either the percentage rise in diastolic pressure during the overshoot phase or the percentage rise in heart rate during the manoeuvre.

Discussion

It was not surprising, in view of the frequent occurrence of left ventricular failure after myocardial infarction, to find 4 patients with the 'square wave' response of cardiac failure; a similar response has been observed in the past in some patients with myocardial infarction (Lee, 1957). The remaining 18 patients, by virtue of the 20 per cent or more reduction in pulse pressure during the manoeuvre, showed their ability to carry out the manoeuvre adequately and that their hearts were capable of responding to a reduced filling pressure. The vasoconstriction and concomitant increase in diastolic pressure during the overshoot phase expected from this reduction in pulse pressure did not occur in 16 patients (89%) implying impairment of the baroreceptor reflex; the remaining 2 had a normal vasoconstrictor response. Further evidence of impaired circulatory reflexes was derived from the failure of the heart rate to increase in response to the fall in pulse pressure during the manoeuvre. The disparity, in three cases, between heart rate response and diastolic pressure response

Fig. 1 Relation between the decrease in pulse pressure during the Valsalva manoeuvre and the increase in pulse pressure in the 'overshoot' phase at the cessation of the manoeuvre. The curved lines represent the upper and lower limits found by Sharpey-Schafer and Taylor (1960) in 360 normal subjects. The open symbols represent 4 patients with a 'square wave' response indicating cardiac failure.

Fig. 2 The relation between decrease in pulse pressure and the increase in heart rate during the Valsalva manoeuvre. The regression line for subjects of a comparable age has been calculated from the data of Gross (1970) and the 95 per cent prediction limits are shown by the broken lines. The open symbols represents the 4 patients with a 'square wave' response, as in Fig. 1.

has been noted in other clinical conditions but its explanation is unclear (Gross, 1970).

There are a number of possible explanations for the impaired circulatory response to the manoeuvre: (1) the effect of age, (2) impairment of nerve transmission, or response, to sympathetic stimulation, or (3) central inhibition of the baroreceptor reflex. The baroreceptor reflex is impaired with ageing (Gross, 1970; Gribbin *et al.*, 1971), but this effect does not appear sufficient to account for these observations in patients with myocardial infarction. It is possible that the baroreceptors themselves could be abnormal after myocardial infarction, and by failing to respond to the reduced pulse pressure result in an impaired vasoconstrictor and heart rate response. Sympathetic nerve transmission and the reactivity of blood vessels is affected by severe metabolic acidosis, hypocapnia, or hypoxia, but as these variables were only marginally abnormal it is doubtful if the reflex was impaired in this way. Very high levels of catecholamines produced by infusion into animals can produce maximum vasoconstriction and thereby prevent any further vasoconstriction in response to the Valsalva manoeuvre (Sarnoff *et al.*, 1948) but the levels of circulating catecholamines after myocardial infarction are unlikely to approach the levels attained during those animal experiments. Significant levels of circulating vasodilators have not been shown in myocardial infarction in man and are an equally unlikely explanation.

The baroreceptor reflex can be suppressed in animals by stimulation of the hypothalamic areas concerned with the 'defence reaction' (Hilton, 1963; Gebber and Snyder, 1970); it is not known whether severe illness in man provokes similar suppression. Reflex inhibition of vasoconstriction has been shown in experimental coronary occlusion in animals (Costantin, 1963; Toubes and Brody, 1970). The inhibitory stimuli are thought to arise in the myocardium or coronary vessels. Myocardial receptors can be shown in animals by histological techniques (Hirsch and Borghard-Erdle, 1961) and by recording impulse activity in the afferent nerves of the heart (Paintal, 1963; Sleight and Widdicombe, 1965; Malliani *et al.*, 1972; Öberg and Thoren, 1972). Similarly, receptors have been shown in coronary vessels (Brown, 1967). Whether similar receptors and reflexes exist in man is unknown but if they do so a similar reflex inhibition could account for the present finding.

The impairment of circulatory reflexes after myocardial infarction may be a factor in causing hypotension, and when cardiac output is reduced by arrhythmias it may explain the rapid deterioration of these patients. Furthermore, it is important to

avoid rapid changes in posture during transportation as these patients will be unable to adjust the circulation as quickly as normal subjects. Recent work has been concerned with the parasympathetic nervous system and its role in arrhythmias (Webb *et al.*, 1972), but the findings presented here suggest impairment of the function of the sympathetic nervous system also.

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