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Severe acute myocardial infarction treated with hyperbaric oxygen

Report on forty patients

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Summary

Forty patients, aged 35–72, who had had an acute myocardial infarct in the preceding 24 hr, and who were seriously ill, were treated in a hyperbaric oxygen bed at 2 atm (atmospheres) absolute for sessions of 2 hr in and 1 hr out for an average period of 4 days.

There were thirty-seven survivors after the treatment, giving an immediate mortality of 7·5%, but three of those died later before leaving hospital, giving a total mortality of 15% in seriously ill patients.

Pain and dyspnoea were usually improved in the first hyperbaric session, relapsed in air and progressively improved in successive sessions.

Arrhythmias, including heart block, showed similar benefit. No case of cardiac arrest occurred while the patients were actually receiving hyperbaric oxygen.

There was, in the opinion of the authors, during a period of over 2 years' experience, a consistent pattern of improvement over and above that expected as spontaneous improvement.

The hyperbaric oxygen bed is a promising method of treatment for the acute phase of myocardial infarction, and it is simple to use. There will of course always be an irreducible minimum of patients who will die from obstruction of both coronary arteries or other structural lesions such as rupture or emboli.

Introduction

Acute myocardial infarction is still one of the commonest lethal diseases remaining unchecked. Even of the patients who reach hospital, approximately 25% die within the next 6 weeks. The circulatory crisis following infarction presents in several ways, and is sometimes remarkably delayed, but patients with signs of left ventricular failure, or with shock, or with an arrhythmia, are hypoxaemic to varying degrees, which aggravates the situation. Although central hypoxaemia may not necessarily be the prime cause of any particular feature of the circulatory crisis, it certainly goes hand in glove with it (MacKenzie *et al.*, 1964; Valentine *et al.*, 1966). To correct this important deficiency high tensions of oxygen must be inspired, because the alveolar–arterial gradient steepens in acute heart failure, and pulmonary shunting reduces the number of alveoli perfused (McNicol *et al.*, 1965). If the arterial hypoxaemia is abolished, the first step in restoring normal tissue metabolism has been taken, and improvement in some aspects of shock could be looked for. Secondly, there is evidence that the pulmonary oedema of left ventricular failure improves with adequate oxygenation (McNicol *et al.*, 1965), and thirdly, protection from ventricular fibrillation after coronary occlusion in dogs is provided by hyperbaric oxygen (Smith & Lawson, 1958; Kuhn *et al.*, 1965; Peter *et al.*, 1966).

This paper describes the technique and results of treating forty patients who were severely ill from acute myocardial infarction, with pure oxygen at 2 atm. The main object was to observe the clinical effects, and to find out whether the method was easy to use. A special hyperbaric bed was available to give oxygen under pressure, so that the therapy could be given as often as required without moving the patient. Moon, Williams & Hopkinson (1964) described the successful treatment of a patient with myocardial infarction, using a small cylindrical hyperbaric oxygen chamber, but the patient was confined in the lying position, and had to be moved to and from his bed for the treatments.

Method

Patients were accepted for treatment who had had an acute infarct in the preceding 24 hr, who were

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not over 75 years old, and who were seriously ill with significant symptoms and signs at the time treatment started. Four patients had already had ventricular defibrillation (Table 1). After clinical examination the patient was placed in the hyperbaric bed, which is a new apparatus designed and made by Vickers Medical. This consists of an ordinary bed on a metal base, with a hinged lid. When the lid is closed the joint is gas-tight, and the bed becomes a compact horizontal pressure chamber. The air is flushed out with oxygen, and the pressure rises to 2 atm absolute, i.e. 15 lb/in^2 (1520 mmHg). An adjacent console contains the valve gear and oxygen conditioner, and is connected to the bed by flexible tubing. The circulation of oxygen is by a closed circuit, and the conditioner absorbs carbon dioxide and maintains any required temperature and humidity. The working is automatic, the operator simply selecting compression or decompression as required. The patient can see through a large Perspex dome at the top end of the bed, and he can communicate by means of a microphone and loudspeaker built into the lid. There is room for the patient to adopt any position in comfort, and the bed itself can be tilted hydraulically. A detailed description of the structure and operation of the hyperbaric oxygen bed is given in the previous paper (Ashfield & Drew, 1969).

Before the first oxygen session, a chest X-ray and an arterial blood sample are taken, and connections are made to an ECG oscilloscope and direct writer. A sphygmomanometer cuff which can be inflated from outside, is applied, and a microphone is placed over the brachial artery. The lid of the bed is then closed and locked electrically. The enclosed air is flushed out and replaced by oxygen, after which the pressure is slowly raised to 2 atm absolute. This is maintained for as long as is required, after which decompression takes place and the lid opened to the air. The usual exposure to the hyperbaric oxygen is 2 hr, including 10 min each for compression and decompression. The hyperbaric oxygen session is followed by 1 hr in air at atmospheric pressure, completing a 3-hr cycle which is repeated continuously over an average period of 4 days. The electrocardiogram is monitored continuously, and pulse rate, blood pressure and respiratory rate are recorded at intervals. Further blood gas analyses and chest X-rays are done on subsequent days. The patient is nursed on the hyperbaric bed, and does not have to be moved.

Results

Forty patients were treated, thirty-six men and four women, with an average age of 56 in both sexes (Table 1). The results are assessed as follows: the effect on symptoms, the effect on clinical signs and measurements, the number of survivors immediately after the treatment and the number surviving to be discharged.

Effect on symptoms

Pain. Twenty-three patients had severe central chest pain, eight moderate, seven mild and two none, at the time treatment started. Within the 1st hr of treatment in hyperbaric oxygen complete relief of pain was obtained in the majority of patients but a few patients had some residual pain which was never bad enough to require analgesics. A striking feature was the satisfactory effect in the more severe cases; the worse the pain was, the more the hyperbaric oxygen seemed to help. When the treatment session was ended and the patient was back in air, the chest pain often returned, but it was easily relieved again by continuing the hyperbaric oxygen immediately. After the second or third session the pain would be subsiding naturally, and the normal interval between sessions could be maintained.

Dyspnoea. Fourteen of the forty patients had dyspnoea bad enough to make it their dominant symptom, and all fourteen had pulmonary oedema clinically. The effect of the hyperbaric oxygen on this symptom was invariably satisfactory, and occurred early in the treatment cycle, usually after about 30 min. Although the subjective relief was rapid, it was found that the clinical signs resolved only after a further interval of several hours, and radiological clearing took even longer. In the worst cases dyspnoea returned whenever the patients were in air, but it was always relieved by giving more hyperbaric oxygen, and as with the effect on pain the relief lasted longer as they improved.

Effect on signs

Pulse rate. In patients with sinus rhythm, hyperbaric oxygen invariably caused a slight slowing of rate. Slowing was sometimes exaggerated during the first sessions by other factors, such as relief of symptoms which often resulted in the patient going to sleep, or at least becoming quiet.

Blood pressure. When in the hyperbaric oxygen the patient showed a small but consistent rise in both systolic and diastolic pressures. This effect was seen in normotensive and hypotensive subjects. In the latter group there was a steady return to normal levels as treatment continued.

Respiratory rate. In the absence of dyspnoea there was no consistent change in rate, but in patients with dyspnoea of left ventricular failure hyperbaric oxygen caused a marked reduction in respiratory rate.

TABLE 1. Thirty-four patients who survived for discharge

Case no.	Age	Sex	Before hyperbaric oxygen					Site of infarct
			Blood pressure	Shock	Pulmonary oedema	Arterial oxygen saturation (%)	Arrest	
1	54	M	80/0	+	+			Ant.
2	44	M	110/60					Post.
3	59	M	130/85			74		Ant.-sep.
4	54	M	100/0		+	96		Post.
5	57	M	90/60	+		79		Post.
6	51	M	90/70	+				Ant.-sep.
7	42	M	125/75					Sep.
8	55	M	90/70			92		Post.
9	59	F	110/50			86		Ant.-sep.
10	56	M	150/100			96		Ant.
11	63	M	160/90					Post.-lat.
12	54	M	110/50	+		71		Post.
13	51	M	140/80			96		Post.
14	66	M	150/95					Ant.
15	52	M	70/0	+	+			Ant.
16	50	M	125/80			97		Post.
17	69	M	95/60			85	VF	Ant.-sep.
18	65	M	100/60	+	+	84		Post.
19	51	M	95/0	+	+			Ant.
20	62	M	100/0		+	82	VF	Ant.
21	55	M	100/50		+	75		Ant.-lat.
22	60	M	80/0			72		Post.
23	64	F	80/0	+	+	48		Ant.
24	48	M	110/70			99		Ant.-sep.
25	67	M	115/70			91		Ant.
27	56	M	125/80			95		Ant.-lat.
28	64	M	120/60		+	89		Post.
29	45	M	120/80					Post.
31	63	M	90/50			92		Post.
32	54	F	120/70		+	77		Ant.sep.
34	35	M	105/70					Post.
35	52	M	80/40	+		95		Ant.-lat.
37	53	M	80/0			92	VF	Post.
38	65	M	105/70				VF (3×)	Post.

Ant., Anterior; lat., lateral; Post., posterior; Sep., septal; VF, ventricular fibrillation.

ECG observations. Hyperbaric oxygen produced the following effects:

(1) A slight slowing of sinus rate.
(2) Improvement in conduction time when the PR interval was prolonged; resolution of partial heart block with dropped beats and sometimes removal of complete heart block.
(3) Restoration of sinus rhythm in many arrhythmias.
(4) Reduced incidence of ventricular ectopic beats.
(5) Transient improvements in early ST segment deviation but no lasting effects, and no change in Q waves nor in other parts of the QRS complex.

Chest X-ray film. The resolution of radiological pulmonary oedema occurred regularly after hyperbaric oxygen and it was found that this took place considerably later than the clinical resolution, the usual interval being about 24 hr, but in one case it was 48 hr. There were no other radiological changes after treatment, and no areas of consolidation or collapse were found.

Blood gases. Twenty-nine patients had an arterial sample analysed for oxygen saturation before treatment began. Nine of these had a saturation greater than 95%, the mean value being 96%. The remaining twenty patients were desaturated, the mean value being 82%. Owing to the extremely grave condition of many of these patients they were installed in the hyperbaric bed as soon as possible; it was not considered justifiable to delay this action to obtain detailed blood gas analysis, and the results of these are not complete enough to draw conclusions in this initial series.

Cardiac arrhythmias. Disturbances of cardiac rhythm and conduction were often observed on the monitoring oscilloscope, especially during the first 48 hr after admission. Only one patient (Case 29)

actually arrested while undergoing the treatment and he was in air at the time, between hyperbaric sessions. A sudden increase in ventricular ectopic beats took place which quickly turned to ventricular tachycardia and then to ventricular fibrillation. Thirty seconds later he had a fit and became unconscious, when external cardiac massage was applied. Two minutes after that he reverted to sinus rhythm spontaneously, so no further resuscitative measures were needed and the lid of the bed was closed and hyperbaric oxygen restarted immediately. He regained consciousness at once and the ventricular ectopics which then returned, gradually disappeared as the session continued. The patient recovered with no further complications. One patient (Case 12) was in well established atrial flutter before receiving his first session of hyperbaric oxygen, and reverted to stable sinus rhythm 30 min after this was started. Two other patients (Cases 37 and 38) were in atrial fibrillation before treatment started, having received electric defibrillation for ventricular fibrillation; both returned to sinus rhythm in hyperbaric oxygen. In one patient atrial fibrillation persisted (Case 25). Another patient (Case 31) developed second degree heart block with the Wenckebach phenomenon, on the 3rd day after the infarct. He was put in hyperbaric oxygen and normal conduction returned in a few minutes. On returning to air the heart block reappeared almost immediately, so hyperbaric sessions were continued in the usual way. Normal conduction was present every time he was in the oxygen and as treatment went on it lasted for longer periods in air. After 36 hr conduction remained normal and subsequent recovery was uneventful.

Side-effects of hyperbaric oxygen at 2 atm absolute

Considering the total duration of the treatment, a certain amount of trouble with oxygen toxicity was expected, and signs of it were looked for. In fact nothing abnormal occurred, and this was probably due to the comparatively low pressure used, and to the intermittent exposure to the oxygen, alternating with air at atmospheric pressure. In particular, there were no symptoms of damage to the central nervous system, and no clinical or radiological evidence of pulmonary collapse or consolidation. In addition, there was no interference with serum electrolytes (sodium, potassium and chloride) or blood sugar, and the effects on arterial gases were beneficial. There were no major complaints from the patients. No claustrophobia occurred, though naturally as they got better they preferred to have the bed open rather than closed.

Survivors

There were thirty-seven immediate survivors (Table 1) out of the forty cases. Three patients died at an early stage (Table 2). One was a man of 72 who had such bad pulmonary oedema that hyperbaric oxygen was started as a final attempt to save him. The pulmonary oedema improved dramatically during the first session, but 9 hr later he developed asystole while in air awaiting his fourth hyperbaric session. An autopsy was not obtained. The second death occurred in a woman of 47. When treatment started she was shocked. She came out of shock but 3 days later, while still receiving hyperbaric oxygen treatment, she collapsed while in air and the heart went into asystole. Autopsy showed that the myocardium was extensively infarcted and both main vessels were blocked by thrombus. The third death occurred in a man of 70 who developed ventricular fibrillation during an attempt to position a pacing catheter in the right ventricle. After resuscitation the catheter was withdrawn and hyperbaric oxygen was used in an attempt to improve conduction. However, a few hours later he died in asystole and autopsy revealed that both main coronary arteries were blocked by thrombus.

Three other patients (Table 2) were immediate survivors, but died 10, 3 and 15 days later, the second of them after a tracheostomy for respiratory insufficiency having initially recovered from partial heart block, and the other two after fresh myocardial infarctions.

Other medical treatment

This was kept to the minimum in order that observations made before and after the hyperbaric therapy would be the more valid. Owing to the rapid effect of this therapy on the patients' pain and also on the pulmonary oedema, shock and arrhythmias, there was no need for analgesic, anti-failure, vasoconstrictor or eurrhythmic drugs. Amylobarbitone, 50–100 mg orally, up to three doses daily, was prescribed whenever a patient was too talkative, unduly anxious or restless. At the specific request of the physician in charge, however, thirteen of the patients were anti-coagulated with heparin during their period of treatment, and all these proved to be in the immediate survivor group. The three patients who died early did not receive heparin and in two of them autopsy indicated that a new thrombosis had supervened in the coronary artery which one could assume had remained patent at the onset of the illness. It is felt that heparin given during the acute phase may at least protect against this complication at a stage when the slightest further thrombosis may mean death. Hyperbaric oxygen is not known to affect blood clotting.

Discussion

The patent with a myocardial infarct faces two main risks to life: the onset of a fatal arrhythmia and

TABLE 2. Deaths

Case no.	Age	Sex	Before hyperbaric oxygen: Blood pressure	Shock	Pulmonary oedema	Arterial oxygen saturation (%)	Site of infarct	Remarks
Early deaths								
26	72	M	120/80		+	85	Lateral	Initially pulmonary oedema improved: asystole while awaiting fourth HBO session. No autopsy
39	47	F	80/0	+	+	82	Ant.	LBBB: 3rd day, asystole. Autopsy, both coronary arteries blocked
40	70	M	0/0	+		95	Ant.	Complete heart block: pacing attempted but VF: defibrillated to sinus rhythm then HBO given: asystole at 16 hours after 5 HBO sessions. Autopsy, both coronary arteries blocked
Late deaths								
30	58	M	110/60			96	Post.	Initially recovered: 10 days later asystole. Autopsy, fresh infarct
33	37	M	85/0	+	+	85	Post.	Initially recovered from partial heart block: tracheostomy with IPPR on 5th day: 8th day, asystole. Autopsy, both coronary arteries blocked
36	61	M	100/65		+	86	Post.	Initially recovered from complete heart block: 15 days later, VF: defibrillation failed. Autopsy, fresh infarct

Ant., Anterior; Post., posterior; HBO, hyperbaric oxygen; IPPR, intermittent positive pressure respiration; LBBB, left bundle branch block.

the effects of an impaired circulation. As yet there is no way of preventing infarction or of reversing the muscle damage that results, but the acute circulatory crisis that may arise is amenable to treatment.

From the anatomical point of view there is one basic fault, namely blockage of an artery to the permanently working muscle, with no immediately adequate collaterals. As a result, ischaemia kills the muscle in the main area supplied, with increasing escape at the infarct boundary. Despite the infarct the rest of the myocardium compensates to a varying degree providing the infarct does not rupture. The risk of a fatal arrhythmia, however, remains, and the commonest one, ventricular fibrillation, is initiated by ectopic foci in the ischaemic transitional zone at the infarct periphery (Harris, 1950). The reduced blood supply to this critical area causes hypoxia, which not only renders the normal conducting system less stable (Baker, 1930), but favours the production of ventricular arrhythmias (Wiggers, Wegnia & Pinera, 1940). This effect may be abolished by using hyperbaric oxygen to obtain the maximum level of the gas in the ischaemic tissue.

The second main risk after myocardial infarction is that of developing an impaired general circulation, and this consists of two factors, a decreased absolute output and decreased pulmonary efficiency (Thomas, Malmcrona & Shillingford, 1965). Both these factors are caused by failure of the left ventricle resulting in raised left atrial and pulmonary venous pressures. When the pulmonary venous pressure reaches a certain critical point pulmonary oedema is obvious clinically, and the patient is recognized as having left ventricular failure, but a falling arterial oxygen reveals that the failure occurs substantially before this. The circulatory crisis after myocardial infarction can thus be self-worsening, with reduced ventricular pumping as the starting cause, leading to hypoxaemia which affects myocardial efficiency, as well as increasing the risk of ventricular fibrillation.

Under certain conditions of lowered cardiac output the patient has a very low systolic blood pressure, cold extremities, and is commonly described as shocked. The vasoconstriction is secondary to the hypotension and results in tissue hypoxia, which in turn causes metabolic acidosis (Kirby & McNicol, 1966). This is not only harmful to the myocardium directly, but also leads to dilatation of the capacitance vessels and therefore to reduced venous return. Cardiac output is further reduced as a result. This vicious circle, involving the weakening ventricular pump, has proved extremely resistant to treatment (Shillingford & Thomas, 1967). The hypoxaemia, however, can be corrected if enough oxygen can be put into the diminished output of arterial blood

(Cameron *et al.*, 1966). Administering the gas as a supplement to the inhaled air by mask or tent, is only really effective when the hypoxia is slight, and under ward conditions oxygen administration is commonly observed to be far from perfect. The hyperbaric oxygen bed solves this problem by ensuring that the gas is given in the highest possible concentration that is known to be safe when continued in regular treatment cycles over several days. In the hyperbaric bed, with the oxygen at twice atmospheric pressure, the partial pressure of the gas is twice 760 mm, viz. 1520 mm, minus about 100 mm for CO_2 and water vapour. The partial pressure achieved in arterial blood depends on ventilation and on the alveolar–arterial gradient. As well as the greatly raised tension of oxygen in the blood there is a substantial increase in the oxygen content, which is first restored to the normal maximum of 20 ml/100 ml by fully saturating the haemoglobin, and then raised a further 4·5 ml/100 ml by solution in the plasma. The vicious circle is thus broken at the arterial hypoxaemia stage; the first benefit is to the myocardium itself, the normal tissue then receiving fully oxygenated blood and the important transitional zone around the infarct becoming less hypoxic. Peripherally, the oxygen has a vasoconstricting effect and the systemic vascular resistance rises. This causes the systolic and diastolic blood pressure to rise, which results in an increase in coronary artery flow which is to a certain extent pressure-dependent. Cameron's work with humans shows that the rise in arterial pressure is achieved despite a still slightly reduced stroke-volume and a slightly reduced cardiac output (Cameron *et al.*, 1966). In those cases which had a metabolic acidosis the hyperbaric oxygen caused a fall in arterial lactate, so tissue perfusion must have been improved or the blood that did get through was carrying enough oxygen to restore normal metabolism. In treating this aspect of shock, high tensions of oxygen have a theoretical advantage over methods directed to increasing the cardiac output by stimulating the myocardium to do more work, since the cells will receive more oxygen even if tissue perfusion is not increased.

The patients we selected for this initial series were all severely ill clinically, and the effect of hyperbaric oxygen could be followed more accurately than would have been the case in patients with paucity of symptoms and signs. Cycles of oxygen treatment (2 hr) alternating with periods in air (1 hr) enabled us to observe whether changes in symptoms and signs during hyperbaric oxygen treatment reverted when the patient was back in air, and returned during further treatment. The continuation of such cycles of oxygen and air over several days was intended to cover the period of circulatory crisis, and as no drugs affecting cardiac failure, arrhythmias or shock were given, the effect of oxygen could be fairly accurately assessed compared with the natural expectation of progress otherwise. Detailed studies made in Glasgow (Cameron *et al.*, 1966) on ten cases of acute myocardial infarction revealed haemodynamic and metabolic results in the same environment as ours. Although their results are very valuable, their patients received only a single treatment session and this could not be expected to cause any sustained clinical change.

We conclude that when hyperbaric oxygen at 2 atm absolute was given to our patients there was a beneficial effect on the symptoms of pain and breathlessness, and on the signs of left ventricular failure, shock and certain arrhythmias. There was a tendency to relapse when the patients were back in air, which we consider strengthens the argument that the hyperbaric oxygen was beneficial. On continuing the treatment over an average of 4 days it appeared that the good effects could be maintained until the immediate crisis was over. The immediate mortality, that is up to the end of the hyperbaric oxygen treatment, was 7·5%. As all the patients were selected because they were seriously ill, this is a satisfactory result. There is no evidence, so far, that the therapy provides benefit after the course is complete, and we were not surprised that three of our survivors sustained fresh myocardial infarcts, at 10, 3 and 15 days after their initial attacks. As it happened hyperbaric oxygen was not used again in these patients, all three of whom subsequently died. If these post-treatment deaths are included the overall mortality was 15%.

We think that the use of frequent, intermittent sessions of hyperbaric oxygen at 2 atm, during the acute phase of the circulatory crisis, shows promise of being a significant advance in treatment.

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