HYPERBARIC OXYGEN THERAPY IN CHRONIC PERIPHERAL VASCULAR DISEASE

By

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Abstract

40 cases of chronic peripheral vascular disease of varying severity were treated with hyperbaric oxygen. The patients were exposed to 2.5 absolute atmosphere for 90 minutes daily to a total of 36 exposures. 37 cases showed improvement of varying degrees. The results are compared with the observations made on 7 control cases.

Introduction

Hyperbaric oxygen (HBO) is being used today in a variety of clinical and pathological conditions associated with reduced O_2 supply to the tissues.[3,4,6,9,11,12,13,14,15,18,20,21,22,24]

While breathing air at sea level, PO_2 in alvepoli is approx. 100 mm Hg. At this pressure, haemoglobin gets approx. 97% saturated with O_2 and carries 19.5 vol. % O_2, while 0.3 vol. % O_2 is dissolved in physical solution. If 100% oxygen is breathed at a pressure 2.5 times the atmospheric pressure, PO_2 in alveoli will amount to approx. 1,800 mm Hg. This pressure of O_2 will saturate the haemoglobin to 100% (20 vol. %) and increase the O_2 in physical solution to 5.5 vol. %. Besides the increased quantity of O_2 available, the PO_2 gradient between arterial blood and the tissues is increased to a considerable magnitude to overcome tissue hypoxia.

The use of hyperbaric oxygen as a mode of treatment in chronic peripheral vascular disease is based on the assumption that the local tissue ischaemia due to restriction of peripheral blood supply or to disturbance of collateral circulation may be overcome by increased availabillity of oxygen in the physically dissolved state under hyperbaric conditions. Illingworth[10] has reported encouraging results in the treatment of limb ischaemia with HBO. Koomen[13] has treated 30 cases of chronic peripheral arterial disease with HBO therapy and reported success in a majority of these cases. Slack *et al.*,[19] on the other hand, reported disappointing results on a series of cases treated with daily exposures of HBO for 1 to 2 hours. Such results might be due to insufficient exposure schedule[6]. However, there is no way of predicting whether a patient can be effectively treated with HBO.

In order to evaluate the role of HBO in cases of chronic peripheral vascular

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disease, the present study was undertaken to determine—

(*a*) the relief of ischaemic pain following HBO therapy;

(*b*) the healing of ulcers not responding to other methods of treatment.

Method

40 cases were selected at random without any consideration of duration of disease, severity of pain, presence of ulcer in the affected limb or previous treatment with lumbar or periarterial sympathectomy.

Before the onset of HBO therapy, clinical examination was made to assess the arterial pulsations, ulceration, complications in the respiratory and the central nervous system. Baseline records of vitalograph, skin temperature and bicycle ergograph were taken. Cases without any pulmonary complications were exposed to high pressure in the hyperbaric chamber with the help of compressed air. The patients breathed 100% oxygen with the help of oxygen masks having non-return inspiratory and expiratory valves. This method not only prevented the wastage of oxygen but also minimised the risk of fire in the chamber, and excluded the medical observer from high pressure oxygen breathing.

Patients were exposed to HBO at 2.5 absolute atmosphere (ATA) once every day, for 90 mts. for a total of 36 exposures. This dosage of HBO was found to be safe during earlier trials carried out by authors.[8,9] Cases developing upper respiratory catarrh or other complications, which were not congenial to HBO therapy, were temporarily withdrawn till they improved. The treatment was subsequently resumed to a total of 36 exposures. The exposures were then discontinued for 2 months and the patients reassessed after that period. Sedatives and vasodilators were withdrawn during the therapy. 11 cases out of the above were reviewed after a period ranging between 4 to 12 months. Three other cases did not show any subjective improvement within the first 10 days of HBO therapy. They complained of aggravation of pain during the exposure. The treatment was discontinued in these cases.

Seven patients were selected at random as "Control" cases and were given placebo therapy. They were fitted with O_2 mask, and made to breathe air at 1 ATA in the hyperbaric chamber. The total duration of these exposures was the same as that of the "Test" group.

Results

All cases including control group were subjected to clinical examination. Skin temperature and response to Bicycle Ergometry were also carried out on completion of HBO therapy and after eight weeks sick leave.

Relief of Pain

The cases were divided depending on the severity of pain into four grades as follows:

Grade I.—Cases who suffered from pain only after prolonged exertion.

Grade II.—Cases who developed pain after walking a few steps.

Grade III.—Cases who had pain even on rest but the pain was relieved by analgesics.

Grade IV.—Cases who suffered from severe pain on rest not relieved by any drugs.

Based on the above criteria, all the cases were graded at the commencement and on termination of HBO therapy. They were also graded after completion of eight weeks sick leave. Results are given at Table I.

TABLE I

Cumulattve Frequency of Decrease in Pain Severity in 37 Test Cases

(n=37)

Before treatment		*After HBO therapy*				*After sick leave*			
		Severity of pain				*Severity of pain*			
Severity of pain	No. of cases	0	Gd. I	Gd. II	Gd. III	0	Gd. I	Gd. II	Gd. III
Gd. IV	7			4	1	1	2	3	1
Gd. III	14	7	4	3		9		4	1
Gd. II	8	7				7	1		
Gd. I	8	6		2		7		1	

TABLE II

Cumulative Frequency Decrease in Pain Severity in 7 Control Cases

(n=37)

Before treatment		*After placebo therapy*			*After sick leave*		
		Severity of pain			*Severity of pain*		
Severity of pain	No. of cases	0	Gd. I	Gd. II	0	Gd. I	Gd. II
Gd. II	4	1	2		0	0	4
Gd. I	3	2	1		1	2	

TABLE III

Incidence of Ulcers Cured oa Improved after HBO Therapy in the Test Cases and the corresponding figure in Control Group

Group	*No. of case having ulcers before treatment*	*Number of cases after treament*			*Number of cases after sick leaver*		
		Cured	*Improved*	*Not improved*	*Cured*	*Improved*	*Not improved*
Test (n=37)	12	6	2	4	10	1	1
Control (n=7)	4	1	1	1	1	..	3

Similar grading was carried out for control group and the results are given at Table II.

Subjectively, most of the cases reported considerable relief of pain within first 10 days. Patients who could not sleep well due to constant pain could sleep well without sedation. The improvement continued throughout the period of treatment. Post sick leave review of the test cases revealed a significant improvement. In comparison, the improvement noted in the Control group was found to be short lived and the condition reverted to the pre-treatment level after the sick leave as shown in Table II.

Healing of Ulcer

Majority of the subjects with ulcers on the limbs or toes who were not responding to other methods of treatment earlier, showed healing under HBO therapy. Out of the 12 cases reported with ulcer, 10 cases healed up completely with HBO therapy. One case showed improvement. Cases with gangrene were given antibiotics in addition to HBO therapy. These cases had received antibiotics earlier without any improvement. The response of ulcers in the test and control group is shown at Table III.

TABLE IV

Frequency of Pulsation at Femoral, Popliteal, Tibial and Dorsalis Pedis Arteries of both sides

(*a*) Before and after tratment, and
(*b*) Before treatment and after sick leave in Test cases.

(*a*)

	Pulse Present (+)				Pulse Absent (—)			
	Femoral		*Popliteal*		*Tibial*		*Dorsalis pedis*	
	+	—	+	—	+	—	+	—
Before Treatment	74	—	48	25	25	45	15	55
After Treatment	73	1	52	21	31	39	17	53
X^2	—		0.3 (N.S.)		0.8 (N.S.)		0.04 (N.S.)	

N.S. — Not Significant.

(*b*)

	Pulse Present (+)				Pulse Absent (—)			
	Femoral		*Popliteal*		*Tibial*		*Dorsalis pedis*	
	+	—	+	—	+	—	+	—
Before Treatment	74	—	48	25	25	45	15	55
After Treatment	73	1	60	13	33	37	20	50
X^2	—		4.30*		1.5 (N.S.)		0.6 (N.S.)	

* Significant at P=0.05. N.S.=Not significant.

Arterial Pulse

Peripheral arterial pulsations were noted over femoral, popliteal, tibial and dorsalis pedis arteries before and after the therapy and also after sick leave. The findings are shown in Table IV. The X^2 values indicate that the proportion of popliteal pulsation present (and absent) before the treatment and after sick leave are significantly differentiated, though not immediately after HBO therapy. The frequency of pulsation in the Control group did not show any change of statistical significance at any of the four recording positions.

Skin Temperature

Temperature was recorded for different parts of the body surface and also from the dorsum of the foot. Mean body surface temperature (MBT_R) was calculated according to Ramanathan's formula[16] and the differences between the MBT_R and the foot temperature have been tabulated in Table V and averages determined for "before treatmeant", "after treatment" and "after sick leave" both in Test and in Control groups. The individual variations in temperature differences between "before treatment" and "after treatment" and between "before treatment" and "after sick leave" were subjected to sign Test in both the groups In Test cases the changes in the temperature differences between "before treatment" and "after treatment" though large, were not significant while the changes between "before treatment" and "after sick leave" were found to be highly significant ($P < 0.01$).

Bicycle Ergograph

Bicycle ergograph studies were made on the Test and the control cases. The subjects were told to cycle against a fixed resistance of 40 watts at 30 RPM and the time was noted till they could not continue any further due to pain. Four amputees were excluded from this test. Tables VI and VII show the distribution of bicycle ergograph data before treatment, immediately after treatment and after sick leave. It is seen, that the improvement in performance immediately after treatment in most of the cases of the test group is very conspicuous and is also maintained even after a period of leave Improvement is noted also in the control group after placebo treatment. However this improvement is transitory, and is not seen after the duration of sick leave.

TABLE V

Mean of the Differences between MBT_R and Foot Temperature

Group	*Before treatment*	*After treatment*	*After sick leave*	*Difference between*	
				Before treatment and after treatment	*Before treatment and after sick leave*
Test (n=37)	4.8	3.5	2.9	N.S.	Significant (P 0.01)
Control (n=7)	4.8	4.3	5.8	N.S.	N.S.

(Figures in °C).

TABLE VI

Bicycle Ergograph Data Before Treatment, After Treatment and After Sick Leave in 33* Test Cases

(*a*) *Before treatment and after HBO treatment*

Before treatment		*After treatment (Time to pain in minutes)*						
Time to pain in minutes	*No. of subjects*	0	1–2	3–4	5–6	7–8	9–10	10
0	19	1	6	1	..	2	2	7
1–2	4	..	..	..	..	..	1	3
3–4	2	..	..	..	..	1	..	1
5–6	..	..	..	..	..	..	..	..
7–8	1	..	..	..	..	..	1	..
9–10	6	..	1	..	..	..	..	5
10	1	..	..	1	..	..	..	..
TOTAL ..	33	1	7	2	..	3	4	16

(*b*) *Before treatment and after sick leave*

Before treatment		*After treatment (Time to pain in minutes)*						
Time to pain in minutes	*No. of subjects*	0	1–2	3–4	5–6	7–8	9–10	10
0	19	2	5	2	1	..	..	9
1–2	4	..	..	..	..	..	..	4
3–4	2	..	1	..	..	..	..	1
5–6	..	..	..	..	..	..	..	..
7–8	1	..	..	..	..	..	..	1
9–10	6	..	..	..	1	..	..	5
10	1	..	..	1	..	..	..	..
TOTAL ..	33	2	6	3	2	..	..	20

* The remaining 4 cases were amputees.

TABLE VII

Bicycle Ergograph Datas in 7 Control Cases

(*a*) *Before exposure and after exposure*

Before treatment		*After treatment (Time to pain in minutes)*						
Time to pain in minutes	*No. of subjects*	0	1–2	3–4	5–6	7–8	9–10	> 10
0	..	..	..	..	..	..	..	..
1–2	1	..	..	..	..	..	1	..
3–4	3	..	..	1	..	..	1	1
5–6	..	..	..	..	..	..	..	..
7–8	1	..	..	..	1	..	..	..
9–10	2	..	..	..	..	..	1	1
> 10	..	..	..	..	..	..	..	..
TOTAL ..	7	..	..	1	1	..	3	2

(*b*) *Before exposure and after sick leave*

Before treatment		*After treatment (Time to pain in minutes)*						
Time to pain in minutes	*No. of subjects*	0	1–2	3–4	5–6	7–8	9–10	> 10
0	..	..	..	..	..	..	..	..
1–2	1	1	..	..	..	..	..	..
3–4	3	..	2	1	..	..	..	..
5–6	..	..	..	..	..	..	..	..
7–8	1	..	..	..	1	..	..	..
9–10	2	..	..	..	..	..	1	1
> 10	..	..	..	..	..	..	..	..
TOTAL ..	7	1	2	1	1	..	1	1

11 out of the 37 test cases reported for review later than 2 months (sick leave) after completion of treatment. This period varied from 3 to 12 months with an average of 5 months. None of these cases showed any untoward trend that could be termed different from those cases which turned up immediately after sick leave.

Discussion

The rationale of use of HBO in ischaemic diseases of the limbs is based on the assumption that the tissue activity is greatly hampered by hypoxia due to impairment of circulation. This leads to failure of homeostasis, *i.e.*, supply of nutrient, removal of catabolites and maintenance of tissue pH which is further aggravated during walking, exercise, etc. Though Bird and Telfar[2] demonstrated considerable reduction in blood flow due to vaso constriction in the normal limbs of subjects breathing 0_2 at 2 ATA, it is not known if this occurs also in ischaemic limbs. Even if it does, the excessive amount of 0_2 carried in physical solution would more than compensate for this reduction in blood flow. The partial pressure of 0_2 in plasma will amount to approx. 1800 mm Hg at 2.5 ATA. Ackerman[1] has observed with the help of polarographic electrodes that the PO_2 in the muscles of the limbs showed immediate rise with HBO. He has also observed that animals with marginal blood circulations, not sufficient to maintain viability indefinitely, may be benefited with HBO.

It is seen from our present study that the benefit lasts for a considerable period after discontinuance of therapy, as evidenced by the healing of ischaemic ulceration, improvement of peripheral temperature and reduction or complete amelioration of pain. The same principle may possibly account for limiting the areas of damage in acute myocardial and cerebral ischaemia[15, 17] restoring the reparative process and thus maintaining the viability of adjacent vital foci.

It is presumed that HBO therapy reduces the state of chronic hypoxia in tissue, maintains its viability and thus allows an earlier development of collateral circulation. It is corroborated by improvement of temperature gradient to the affected limb after the treatment despite the continued absence of peripheral pulsation in leg and foot in most of the cases. Some cases showed reappearance of arterial pulsation in the popliteal arteries suggestive of recanalisation. In thromboangitis obliterans (TAO) the basic pathology is a change in blood vessels characterised by thrombosis, active canalisation and development of a certain amount of collateral circulation, and at times development of excessive elastic tissue in and around the occluded or partially occluded vessels. Dible[7] observes that the process of recanalisation of thrombus is relatively more rapid in TAO than in other forms of peripheral vascular disease, because of the absence of degenerative changes due to age and progressive atheroma. The improvement in pulsation of the popliteal artery noted in the study could be due to the commencement of HBO therapy at the early stage of involvement of the vessel. Failure amongst the cases treated can possibly be accounted for by the advanced stage of disease. It is likely that HBO benefits only those cases which have a moderate obstruction of blood supply and is a complete failure in advanced cases with severe or complete obstruction.

The subjective improvement shown by a few of the control cases can be accounted for by the natural periodicity of the disease process and also by the temporary relief of the psychological element.

Conclusions

The results from the study of HBO therapy on 40 cases of peripheral vascular disease show that the response is significant as is evident by the relief of pain, healing of ulcers and increased circulation in the limb shown by improved temperature gradient. Our study extends to a period of review ranging between 2 to 12 months. Psychological factors play a part in relieving the severity of symptoms as shown by the initial improvement in Control cases, majority of whom later reverted to their original condition once the placebo therapy was withdrawn. Lumbar sympathectomy which is considered a radical treatment besides amputation does not also provide lasting relief. In comparison, HBO therapy has produced an appreciable recovery in majority of treated cases, and varying degrees of relief of severity of symptoms in others.

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