

PAPERS AND ORIGINALS

Long-term Domiciliary Oxygen in Chronic Bronchitis with Pulmonary Hypertension

R. D. STARK, P. FINNEGAN, J. M. BISHOP

British Medical Journal, 1973, 3, 467-470

Summary

Five patients with chronic bronchitis and pulmonary hypertension were treated with oxygen in their homes for periods of between 6 and 24 months. Oxygen was supplied for 15 hours daily from cylinders or from an oxygen concentrator and few practical difficulties arose. After 23 to 59 weeks of treatment there were significant decreases in pulmonary arterial pressure and vascular resistance, and four of the five patients no longer had pulmonary hypertension at rest. Two of these patients had shown little response after three weeks of treatment. There was a reduction in the number of episodes of congestive cardiac failure compared with the corresponding period before treatment. Two of the patients improved enough to return to work. These results are encouraging enough to justify a controlled trial of the treatment in a large number of patients.

Introduction

We showed previously that the pulmonary hypertension of patients with chronic bronchitis was partially reversed by administration of oxygen for 24 hours daily (Abraham *et al.*, 1968) and for 15 hours daily (Stark *et al.*, 1972). These changes were apparent after three to eight weeks of treatment with oxygen but little is known about the effects of prolonged treatment.

The work described in this paper sought answers to three questions. Firstly, is there further reduction in the pulmonary hypertension and in the pulmonary vascular resistance after the first three to eight weeks of treatment? Secondly, is the administration of oxygen in the home on a long-term basis a

practicable proposition? Thirdly, is the decrease in the pulmonary arterial pressure accompanied by an improvement in the clinical condition of the patients and by a reduction in the number of episodes of congestive cardiac failure?

Methods

Five patients with chronic bronchitis and pulmonary hypertension underwent treatment with oxygen in their homes for periods of between six months and two years. The responses after three to six weeks in three of these patients were reported previously (Stark *et al.*, 1972). The principal criteria for selection were hypoxaemia, a history of episodes of congestive cardiac failure, and willingness to participate in the study. The reliability of the patient was an important factor, and though few problems arose the arrangement and situation of the house helped to determine the practicability of treatment with oxygen at home.

Before admission to the trial a full explanation of the treatment was given to the patient on at least two occasions. It was made clear that the treatment was experimental and that we hoped to follow their response by tests of pulmonary function and by measurements during right heart catheterization. The five patients described were willing to participate and gave permission before each procedure.

The patients received diuretics and most took digoxin during the period of study; the treatment was not changed except for the discontinuance of spironolactone in one patient who developed painful gynaecomastia. All patients had a supply of tetracycline or co-trimoxazole at home and started a course at first evidence of a chest infection. Two patients who previously smoked 5 to 10 cigarettes a day stopped smoking at the start of the study. Of the others, two continued to smoke 10 to 20 cigarettes a day and one patient did not smoke.

Investigations were not performed during exacerbations of bronchitis, since this is known to cause a transient rise in pulmonary arterial pressure (Abraham *et al.*, 1969), or during episodes of congestive cardiac failure. The patients were carefully observed for signs of cardiac failure and most weighed themselves daily throughout the study.

The patients received oxygen through nasal catheters (Pharmaseal K29) at a flow rate of 2 l./min for 15 hours daily. Treat-

University Department of Medicine, Queen Elizabeth Hospital, Birmingham B15 2TH

R. D. STARK, PH.D., M.R.C.P., Research Fellow
P. FINNEGAN, M.B., M.R.C.P., Lecturer in Medicine
J. M. BISHOP, M.D., F.R.C.P., Professor of Medicine

ment was undertaken overnight, usually from 6 p.m. until 9 a.m. During the early part of the study one patient took oxygen for only 13 hours a day but thereafter increased to 15 hours a day. The nasal catheters proved to be comfortable over long periods, though each set had a limited life. One patient complained of nasal irritation, but this was abolished after passing the oxygen supply through a water trap, which was thoroughly cleaned and disinfected twice weekly.

Each patient installed a simple, low-pressure system for piping the oxygen to outlets in the bedroom and in the living room. Polyethylene tubing (internal diameter 4 mm) was used for this purpose and was easily concealed close to skirting boards. A three-way tap allowed diversion of the oxygen supply from one outlet to the other. One patient installed an oxygen outlet in the bathroom and one in a greenhouse.

At weekly intervals Vickers Ltd. delivered five or six cylinders each containing 120 ft³ (3.4 m³) of oxygen. The cylinders were accommodated in the upright position in a recess close to the front door, and this minimized the disturbance within the house. The cylinder-head incorporated a flowmeter and was changed and tightened by hand. The volume of oxygen delivered each week was in excess of the patients' consumption, probably due to leakage, and this wastage was at least 25% of the delivered volume. Otherwise the delivery of oxygen produced few problems.

Two patients used cylinders of 48 ft³ (1.35 m³) for part of their treatment which was undertaken at work. One patient received oxygen from an oxygen concentrator (Stark and Bishop, 1973).

With the agreement of the family doctor visits to each patient were made by one of us at intervals of one or two weeks initially and then less frequently. Inquiry was made about the recordings of body weight, the presence of ankle swelling, and the production of purulent sputum.

Pulmonary arterial pressure, pulmonary wedge pressure, and pulmonary blood flow were measured at rest and during submaximal exercise using pressure transducers and the direct Fick method, as described previously (Stark *et al.*, 1972). When technical problems prevented the measurement of pulmonary wedge pressure the mean value from the other studies in that patient was used. All patients were breathing air during the haemodynamic studies and the reduction in pulmonary arterial pressure therefore represented a change in the pulmonary vascular bed which persisted after return to hypoxaemic conditions. Measurements were made immediately before treatment with oxygen started and three to six weeks and 23 to 59 weeks after the start of treatment. Pulmonary function, arterial blood gas tensions, and packed cell volume were measured as described previously (Stark *et al.*, 1972). Student's *t* test was used to determine statistical significance; as before, the single-tail test was used for pulmonary arterial pressure and vascular resistance.

Results

BLOOD GAS TENSIONS

All patients were hypoxaemic and hypercapnic while breathing air (table I). Over the course of the study the mean PaO₂ while

breathing air increased from 46 to 51 mm Hg and the mean PaCO₂ increased from 55 to 57 mm Hg, neither change being statistically significant.

When oxygen was administered the mean PaO₂ increased from 50 to 68 mm Hg and the lowest value was 61 mm Hg (table I). In the first few days of treatment several patients had morning headache due to hypercapnia. Thereafter there was no clinical evidence of hypercapnia, though the mean PaCO₂ was 5 mm Hg higher than during the breathing of air.

PULMONARY FUNCTION

During the period of study vital capacity did not change but there were significant decreases in residual volume (means 5.6 and 4.5 l.; *P* < 0.05) and total lung capacity (means 8.6 and 7.6 l.; *P* < 0.05). Forced expiratory volume in one second showed a downward trend in some patients (table I), but for the group as a whole the change was insignificant. The ratio of forced expiratory volume in one second to vital capacity was unchanged, as was the transfer factor.

HAEMATOLOGY

The packed cell volume decreased in four patients. In one patient there was evidence of iron deficiency due to a previous partial gastrectomy, and treatment with iron was followed by a rise in the packed cell volume (table I). We have no doubt that this patient took the oxygen as instructed. Nevertheless, his modest decrease in pulmonary vascular resistance, the decrease in forced expiratory volume in one second, and the decrease in PaO₂ from 53 to 49 mm Hg raise the possibility that the increase in polycythaemia was associated with deteriorating pulmonary function.

HAEMODYNAMICS

After treatment with oxygen for 23 to 59 weeks mean pulmonary arterial pressure at rest decreased significantly from 34 to 22 mm Hg (*P* < 0.05; see fig., table II). At the final study four of the patients had pulmonary arterial pressures which lay within the normal range (Segel *et al.*, 1964).

After three to six weeks of treatment the decrease in pulmonary arterial pressure was significant (*P* < 0.05), though two of the patients showed no change in pressure. Subsequently one of the two had a decrease in pulmonary arterial pressure and both had sizeable changes in pulmonary vascular resistance. It follows that the response after short periods of oxygen therapy is of limited value in predicting the final response.

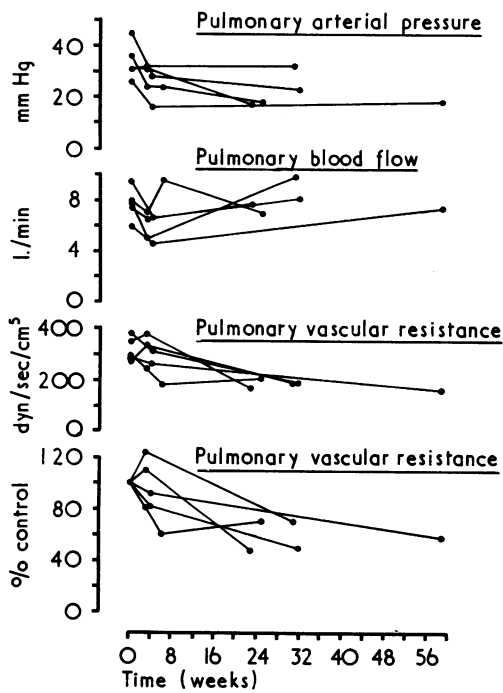
Pulmonary vascular resistance decreased significantly after 23 to 59 weeks of treatment (*P* < 0.05). The change after three to six weeks was not significant but the change between the second study and the final study was significant (*P* < 0.05). No change occurred in pulmonary wedge pressure or in pulmonary blood flow.

For each patient the oxygen uptake during steady exercise was similar, and it was therefore justifiable to compare the haemodynamic studies.

TABLE I—Age, Weight, Respiratory Values, and Packed Cell Volume before and after Various Periods of Treatment with Oxygen

Case No.	Age	Time (Weeks)			Weight (kg)			Mean PaO ₂ (mm Hg)		Mean PaCO ₂ (mm Hg)		FEV ₁ (l.)			P.C.V. (%)		
		1	2	3	1	2	3	On Air	On O ₂	On Air	On O ₂	1	2	3	1	2	3
1	55	0	6	25	82	84	80	53	79	55	60	0.99	1.11	1.16	54	46	40
2	39	0	4	32	86	87	100	45	61	48	56	0.86	0.91	0.84	65	60	59
3	55	0	3	31	74	76	79	49	62	59	54	0.67	0.52	0.45	48	47	59*
4	58	0	3	23	74	75	73	46	67	61	65	0.64	0.55	0.55	53	49	48
5	62	0	4	59	81	78	85	55	73	53	68	0.96	0.96	0.72	59	52	43

* After treatment with ferrous sulphate.
FEV₁ = Forced expiratory volume in 1 second.
P.C.V. = Packed cell volume.



Pulmonary haemodynamic measurements in the five patients studied.

mododynamic data before and after treatment with oxygen (table III). Since the limited exercise tolerance of one of the patients prevented serial studies the data are incomplete and no statistical

analysis was performed. The individual results, however, show that the pulmonary arterial pressure and vascular resistance during exercise were usually lower after treatment with oxygen.

MORBIDITY

At the start of the study one patient had been working in the recent past and four patients had not worked for at least two years. While receiving treatment two of the patients were able to return to work, one full-time and one part-time. The employers of the patient who was working at the start of the study recommended that he retire on medical grounds. Two of the patients did not return to work.

Two patients receiving long-term oxygen each had one episode of cardiac failure as judged by a history of leg swelling, by physical signs of raised jugular venous pressure, hepatomegaly and oedema, and by a rapid increase in body weight. In periods of the same duration before treatment was started there were 11 episodes of congestive cardiac failure in five patients (table IV). There was only one acute admission to hospital for treatment of complications of chronic bronchitis during the period of treatment compared with 10 acute admissions in the corresponding period before treatment. During the trial three patients had an increase in body weight which was not due to retention of fluid.

The number of exacerbations of bronchitis has not proved a useful index of morbidity, since it has been our aim to treat the first evidence of infection. In addition it was occasionally difficult to abolish infection and one exacerbation tended to merge with the next. All patients had a supply of antibiotics at home and were given clear instructions to start a course if they had an

TABLE II—Pulmonary Arterial Pressure (P.A.P.), Pulmonary Wedge Pressure (P.W.P.), Pulmonary Blood Flow (P.B.F.), and Pulmonary Vascular Resistance (P.V.R.) at Rest after Periods up to 29-59 Weeks of Oxygen Therapy

Case	Hours/Day	Time (Weeks)			P.A.P. (mm Hg)			P.W.P. (mm Hg)			P.B.F. (l./min)			P.V.R. (dyn/sec/cm ²)		
		1	2	3	1	2	3	1	2	3	1	2	3	1	2	3
1	15	0	6	25	36	24	18	7	3*	0	7.9	9.5	7.0	295	178	207
2	15	0	4	32	45	28	23	0	2	4	9.4	6.6	8.1	382	313	187
3	15	0	3	31	31	32	32	5	11	9	7.7	5.0	9.8	269	335	187
4	15	0	3	23	31	31	17	-1	0*	1	7.4	6.5	7.7	346	381	166
5	13-15	0	4	59	26	16	18	5	1	3	5.9	4.6	7.3	285	262	164
Mean					34	26	22	3	3	3	7.7	6.4	8.0	315	294	182
		P (1 and 2)			<0.05			>0.05			>0.05			>0.05		
		P (1 and 3)			<0.05			>0.05			>0.05			<0.05		
		P (2 and 3)			>0.05			>0.05			>0.05			<0.05		

* Assumed (see text).

TABLE III—Oxygen Index, Pulmonary Arterial Pressure (P.A.P.), Pulmonary Wedge Pressure (P.W.P.), Pulmonary Blood Flow (P.B.F.), and Pulmonary Vascular Resistance (P.V.R.) during Exercise after Periods up to 23-59 Weeks of Oxygen Therapy

Case No.	Hours/Day	Time (Weeks)			Oxygen Index (ml/min/m ²)			P.A.P. (mm Hg)			P.W.P. (mm Hg)			P.B.F. (l./min)			P.V.R. (dyn/sec/cm ²)		
		1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3
1	15	0	6	25	321	292	326	52	42	27	10	10*	3	11.4	12.5	10.2	294	204	180
2	15	0	4	32	373	356	362	76	51	47	5*	5	5*	11.4	11.2	11.0	499	327	305
3	15	0	3	31	347	—	—	58	—	—	—	—	16	10.0	—	—	335	—	—
4	15	0	3	23	248	238	263	46	53	53	6	8*	9	9.1	10.0	10.9	352	361	322
5	13-15	0	4	59	343	345	348	41	26	35	12	11	11	9.7	8.8	11.2	240	137	172

* Assumed (see text).

TABLE IV—Working History, Number of Episodes of Congestive Cardiac Failure (C.C.F.), and Number of Acute Admissions to Hospital associated with Chronic Bronchitis after and in the Corresponding Period before Treatment with Long-term Oxygen

Case No.	Time since Start of Treatment (Months)	Work in Same Period		Episodes of C.C.F. in Same Period		Acute Admissions in Same Period	
		Before	After	Before	After	Before	After
1	24	0	Full-time	4	0	4	0
2	17	0	0	4	1	4	1
3	12	0	Part-time	1	1	1	0
4	6	0	0	0	0	0	0
5	14	Full-time	Retired	2	0	1	0

upper respiratory tract infection or if the sputum showed traces of purulence. In spite of this and in spite of frequent repetition of the instructions treatment with antibiotics was often delayed.

Discussion

There have been several reports from Denver, Colorado, on the long-term administration of oxygen to patients with chronic bronchitis (Levine *et al.*, 1967; Petty and Finigan, 1968; Neff and Petty, 1970). Oxygen from the Linde liquid oxygen unit was administered in the home for periods up to 41 months. In most studies oxygen was given continuously, partly because bronchitics in Denver have to contend with the additional effect of altitude. In patients with chronic bronchitis and pulmonary hypertension there were decreases in red cell volume and pulmonary arterial pressure and congestive cardiac failure was more easily controlled. When compared with published series of bronchitics not treated with oxygen there was a significant reduction in mortality. In patients with chronic bronchitis who did not have pulmonary hypertension, however, treatment with oxygen failed to reduce mortality (Neff and Petty, 1970).

The present study showed that long-term treatment with oxygen in the home was practicable. Whereas the continuous administration of oxygen described above is very restrictive, the 15-hour regimen can be taken overnight and allows nine hours a day free from either domestic or portable supplies of oxygen. The freedom permits the patient to lead a fuller life and probably leads to greater co-operation from the patient.

Attention was given to the selection of suitable patients and particularly to the supervision of the treatment in their homes. All houses were easily modified to accommodate the supply of oxygen and treatment at home was never prevented on these grounds. The costs of oxygen and the advantages of the domiciliary oxygen concentrator were described previously (Stark and Bishop, 1973). Against the expense of treatment must be considered the reduction in time spent in hospital and the return to employment.

We confirmed our previous finding that oxygen administered for 15 hours daily decreased pulmonary vascular resistance (Stark *et al.*, 1972) and it was shown that reversal of the pulmonary hypertension may continue after the first six weeks of treatment. By 23 to 59 weeks the changes in pulmonary arterial pressure and vascular resistance were statistically significant, and four of the five patients no longer had pulmonary hypertension at rest (table II; Segel *et al.*, 1964).

The haemodynamic response after three to six weeks of treatment gave an indication of the long-term response in three of the patients but was unhelpful in two patients whose responses became apparent only after the first three weeks. Failure to show a response as judged by a fall in pulmonary arterial pressure during the early weeks of treatment does not therefore preclude a satisfactory late response.

Morbidity is difficult to measure. Return to work depends on motivation, availability of jobs, and the attitude of the employer as well as the fitness of the patient. The numbers of episodes of

congestive cardiac failure and of acute admissions to hospital give an indication of morbidity but the interpretation is not simple. A large decrease in such acute episodes occurred after treatment with oxygen, whereas the natural progress of the disease would favour an increase. Exercise tolerance was not measured and further study of this aspect is required. Three patients gained body weight, and this may reflect an improvement in general health.

The symptomatic benefits obtained by some patients may have been due to the treatment with oxygen, but other factors may be important—additional medical attention both in hospital and at home, the placebo effect of oxygen, the closer supervision of the taking of drugs, and the prompt treatment of respiratory infections. All things considered, there is little doubt that reversal of the pulmonary hypertension is related to the effects of oxygen on the pulmonary circulation.

Over the period of study residual volume and total lung capacity decreased significantly. Previously no change in pulmonary function was shown during courses of therapy with oxygen (Abraham *et al.*, 1968; Stark *et al.*, 1972), but in the present instance the study covered a longer period. However, no other evidence of altered respiratory function was obtained and the oxygen and carbon dioxide tensions while breathing air and the forced expiratory volume in one second, the vital capacity, and the transfer factor did not change. There is no obvious explanation for the reduction in residual volume and total lung capacity and further observations are required.

The limitations of the present investigation show the need for a controlled study in a large number of patients; this could best be achieved by a multicentre trial. Both the treated and control groups should be closely supervised and visited at the same frequency. With the demonstration of the haemodynamic effects of oxygen the need is now for a study of mortality, morbidity, and exercise tolerance.

We gratefully acknowledge the help given by all who work in the department of medicine. In particular we are grateful to staff nurse M. Booth, Miss J. Blackhall, Miss F. Langley, Mrs. J. Taylor, and Mr. J. Milton for technical help. Excellent co-operation has been received from the family doctors of the patients, Dr. J. Baker, Dr. N. Blackwell, Dr. J. Bunting, Dr. P. Ireland, and Dr. A. Wardle, and from Vickers Ltd., who delivered the oxygen. The work was supported by grants from the British Heart Foundation and from the Chest and Heart Association.

References

- Abraham, A. S., Cole, R. B., and Bishop, J. M. (1968). *Circulation Research*, **23**, 147.
- Abraham, A. S., *et al.* (1969). *Circulation Research*, **24**, 51.
- Levine, B. E., *et al.* (1967). *Annals of Internal Medicine*, **66**, 639.
- Neff, T. A., and Petty, T. L. (1970). *Annals of Internal Medicine*, **72**, 621.
- Petty, T. L., and Finigan, M. M. (1968). *American Journal of Medicine*, **45**, 242.
- Segel, N., Hudson, W. A., Harris, P., and Bishop, J. M. (1964). *Journal of Clinical Investigation*, **43**, 1541.
- Stark, R. D., and Bishop, J. M. (1973). *British Medical Journal*, **2**, 105.
- Stark, R. D., Finnegan, P., and Bishop, J. M. (1972). *British Medical Journal*, **3**, 724.